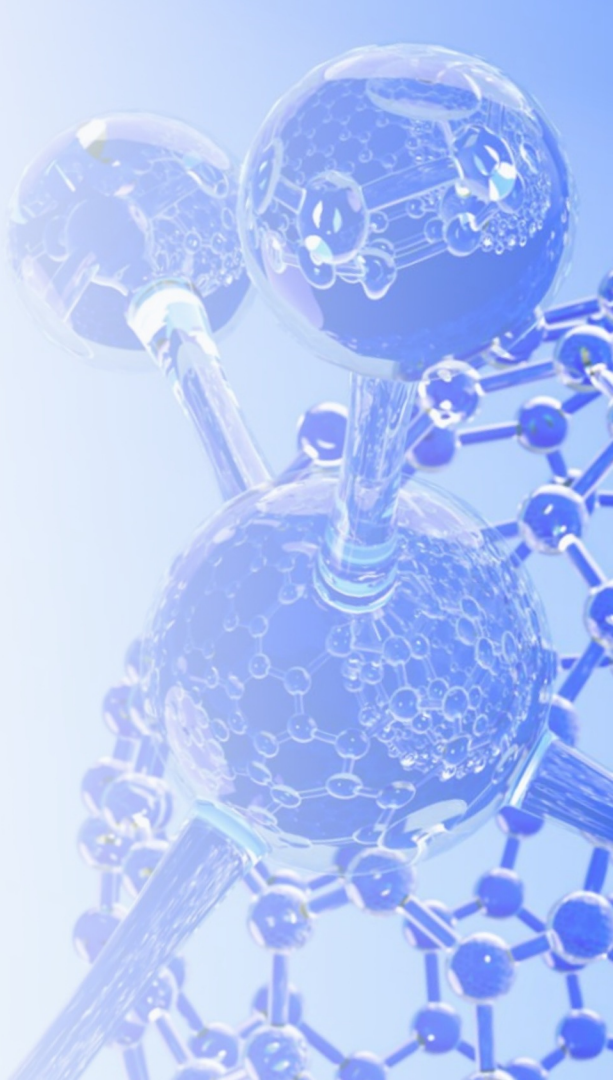
zymeworks

Making a Meaningful Difference

Developing novel medicines for patients with difficult-to-treat cancers and other serious diseases



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)

zymeworks

Integrated R&D Engine

Multispecific Antibody Therapeutics (MSAT)

Antibody Drug Conjugates (ADC)

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

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

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

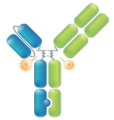
Goal of optimizing value as measured by per share returns for shareholders over the long-term

Jazz Pharmaceuticals

Zanidatamab Collaboration with Jazz Pharmaceuticals

BeiGene

Zanidatamab Collaboration with BeiGene



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

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 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

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)

EFECT™

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

Multispecific

Zanidatamab (ZW25)

Biparatopic anti-HER2

Unique biology lends additional benefit achieved by mAb combinations

Design with Complementary Technology

TOPO1i Platform

ZymeLink™ Auristatin Hemiasterlin

Site Specific Conjugation

TLR7 ISAC

Azymetric™

T cell engagers

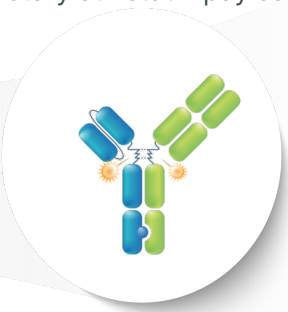
ProTECT™

EFECT™

Antibody Drug Conjugate

Zanidatamab Zovodotin (ZW49)

Biparatopic anti-HER2 with proprietary auristatin payload



Efficient internalizer and payload delivery

Pivotal clinical studies

Goal of 5 **New** INDs in 5 years

Clinical POC study

DAR: drug to antibody ration; 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					BeiGene Jazz Pharmaceuticals
2nd-Line Biliary Tract Cancers HERIZON-BTC-01 Monotherapy					BeiGene Jazz Pharmaceuticals
1st-Line Gastrointestinal Cancers Gastroesophageal Adenocarcinoma, Biliary Tract Cancer, and Colorectal Cancer Chemotherapy Combination					BeiGene Jazz Pharmaceuticals
Zanidatamab Monotherapy & Chemotherapy Combination					BeiGene Jazz Pharmaceuticals

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

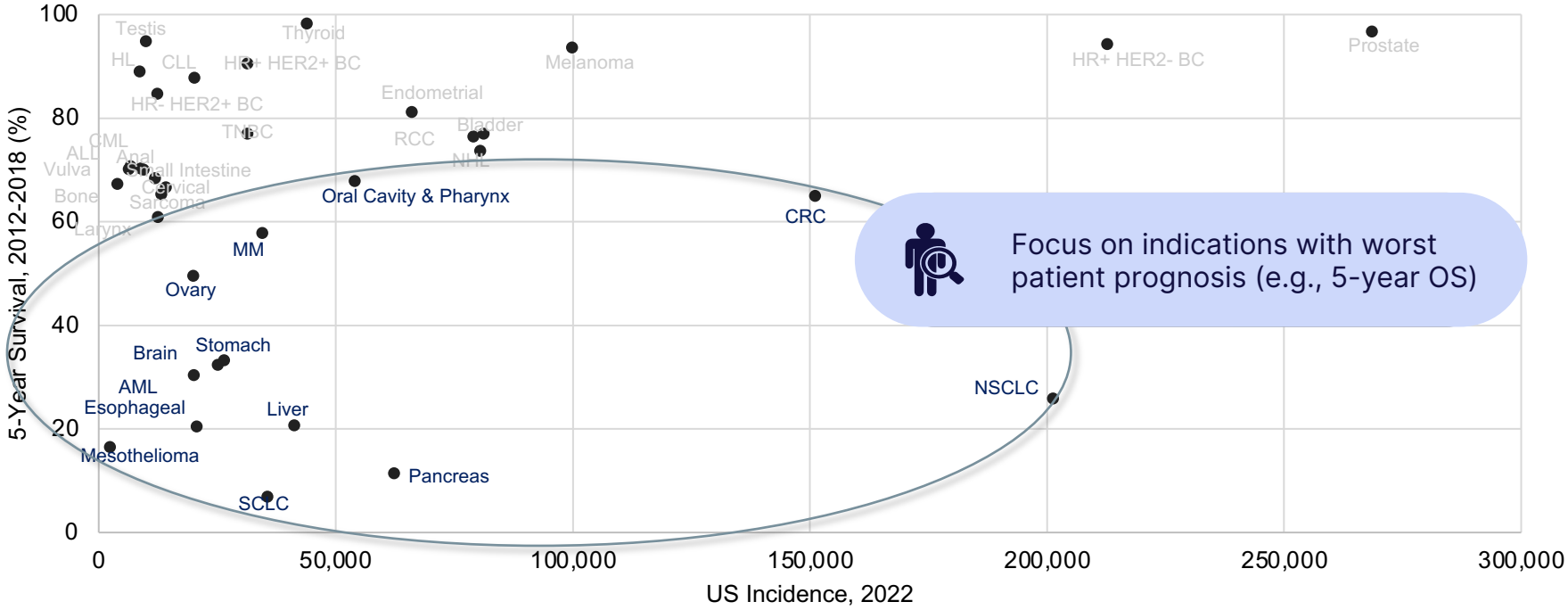
Early Development and Early R&D	Preclinical	Phase 1	Phase 2	Pivotal	Partner
Zanidatamab Zovodotin HER2-Expressing Cancers Indications: NSCLC, GEA, CRC, OVCA, BC					BeiGene
ZW191 Folate Receptor-α Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indications: OVCA, Gynecological, NSCLC					
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

Goal: Focus on Cancer Indications with Greatest Unmet Patient Need

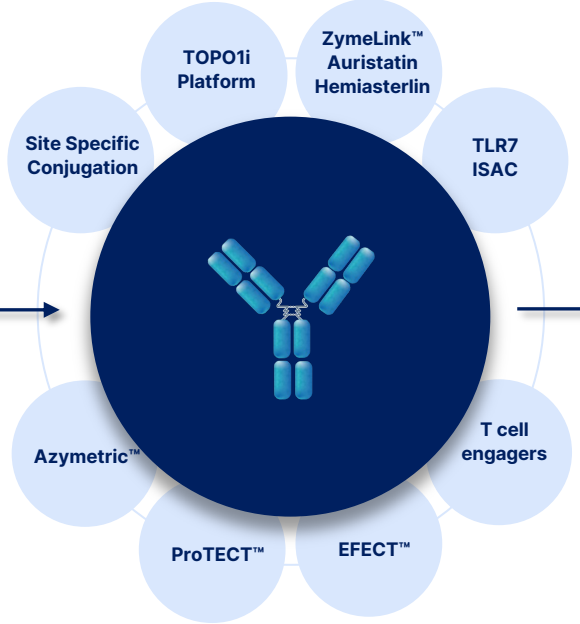


SEER*Explorer, accessed 10 Oct 2022

ADC and Multispecific Modalities Driving Our Pipeline

Select Difficult-to-Treat Cancers & Target

Design with Complementary Technology

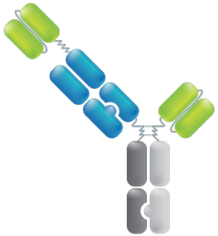


Optionality with Two Foundational Fit-for-Purpose Modalities

Anti-body Drug Conjugates

Customization:

- Antibody properties
- Antibody format
- Payload
- DAR



Multi-specifics

Customization:

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

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

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

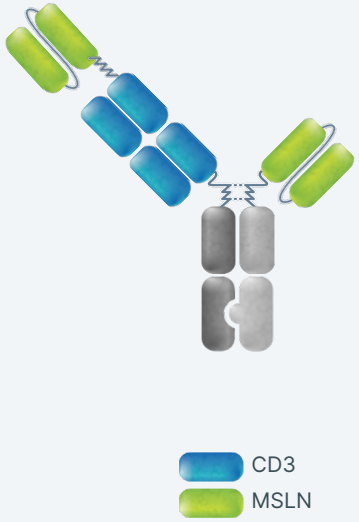
Biological Problem	Zymeworks Solution
1 Narrow therapeutic window and toxicity due to CRS associated with Gen 1 TCE in solid tumors	**2+1 T Cell Engager (ZW171)** Mitigate cytokine release syndrome with low affinity T cell binding and enhanced efficacy and selectivity with avidity-driven tumor antigen binding
2 Limited T cell intratumoral availability and T cell anergy in solid tumors	**TriTCE Co-stimulation** Increase T cell fitness, activation and proliferation via tumor-dependent T cell co-stimulation
3 Immunosuppressive tumor microenvironment limiting T cell responses in solid tumors	**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

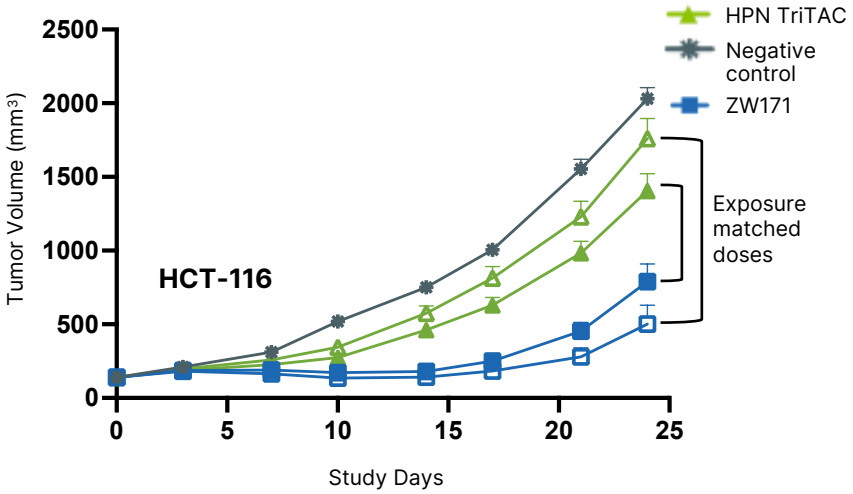
Validation

In preclinical development

Targeting IND 2024

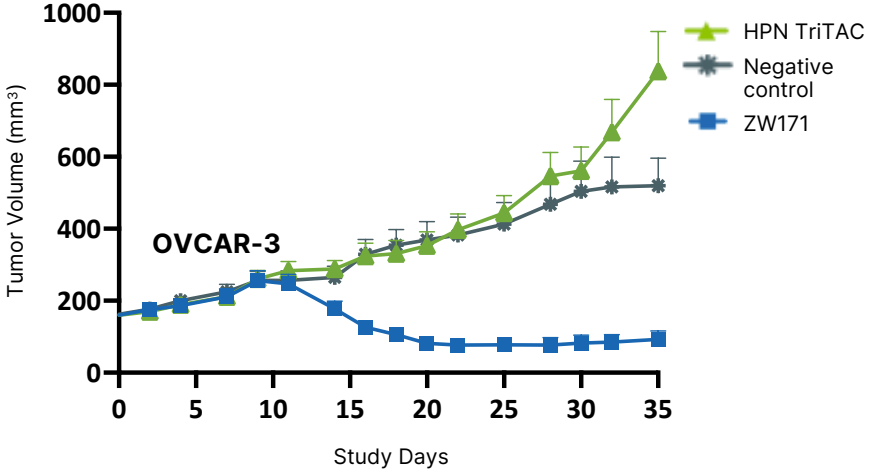
ZW171 Mediates Greater In Vivo Anti-Tumor Activity Compared to Benchmark

In Vivo Anti-Tumor Activity
MSLN^{Mid}-Expressing Colon Cancer Model



NPG mice were engrafted with HCT116 cells and human PBMC (2 donors) intraperitoneally. When tumors reached 100-200 mm³, dosed i.v. QW x4 with ZW171 or i.p. daily x 18 with HPN triTAC. Serum exposure concentrations and matched exposure doses confirmed by PK analysis. Negative control is anti-hemagglutinin x CD3 bispecific.

In Vivo Anti-Tumor Activity
MSLN^{High}-Expressing Ovarian Cancer Model

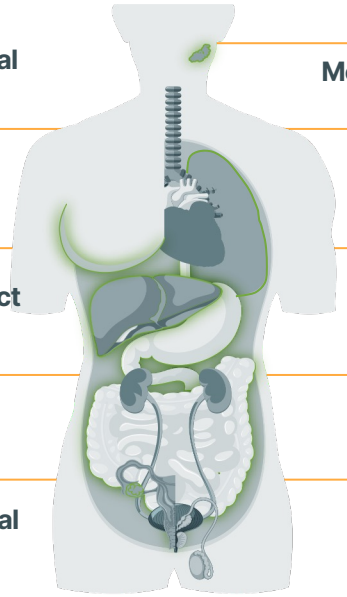


OVCAR-3 tumor fragments were engrafted subcutaneously in NOG mice.
After tumors reached 100-200 mm³, mice were humanized with donor PBMC (3 donors) and dosed i.v. QW x4 with ZW171 or i.p. daily x 18 with HPN triTAC. Negative control is anti-hemagglutinin x CD3 bispecific.

ZW171 Treatment Opportunity

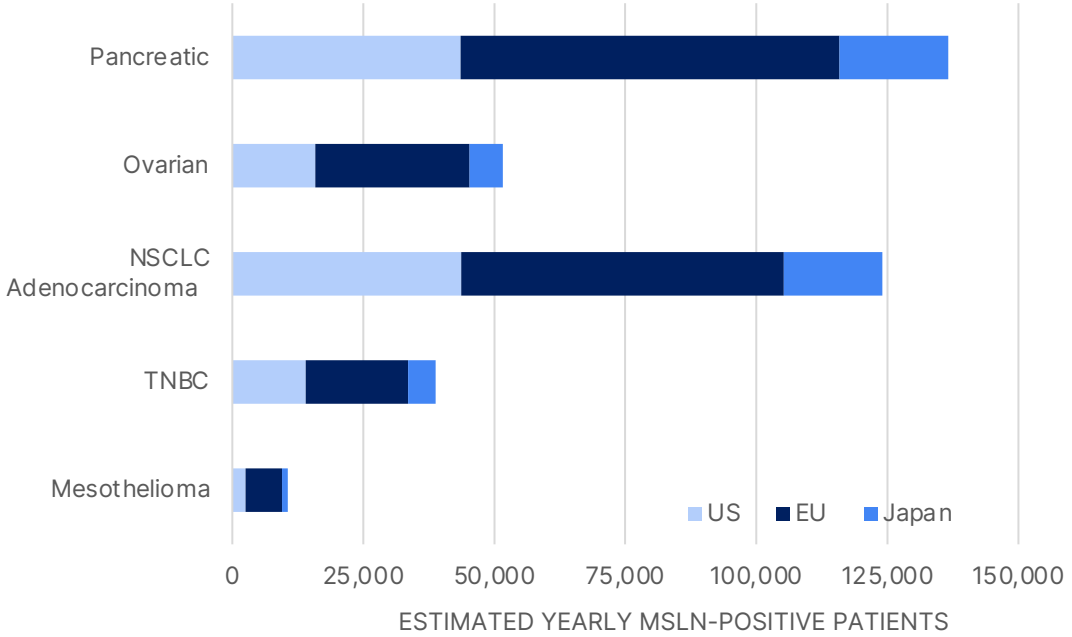
Potential first and best-in-class treatment for MSLN+ pancreatic, ovarian, NSCLC, TNBC, mesothelioma and other MSLN-expressing cancers

MSLN EXPRESSING CANCERS



- Thymic 40-45%
- Esophageal 35-40%
- Mesothelioma 75-80%
- Breast 25-30%
- Lung 60-65%
- Biliary Tract 60-65%
- Gastric 50-55%
- Ovarian 60-65%
- Pancreatic 80-85%
- Endometrial 20-25%
- Colorectal 40-45%

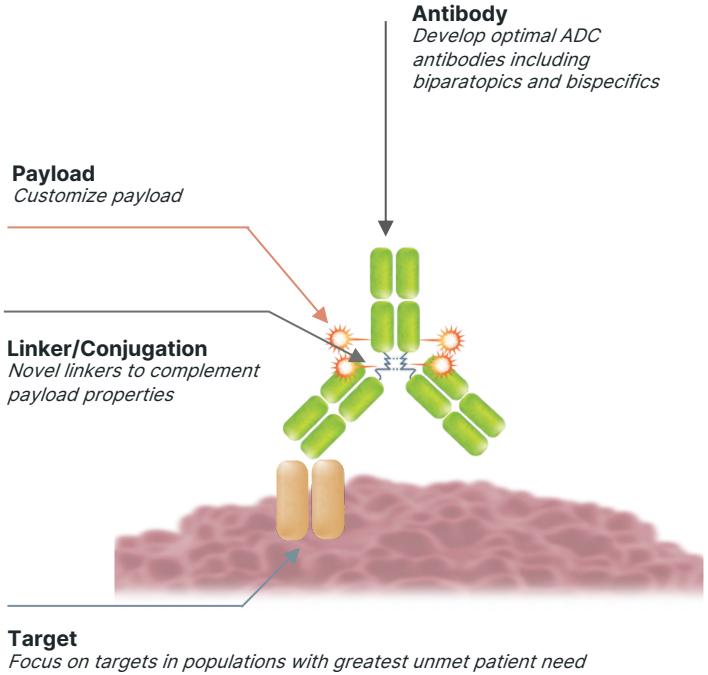
ESTIMATE OF NEWLY-DIAGNOSED MSLN+ PATIENTS IN KEY INDICATIONS



Modified from Morello et al Cancer Discovery; Vol. 6 Feb 2016 and Inaguma et al Oncotarget; Vol 8 Apr 2017
NSCLC: Non-small cell lung cancer; TNBC: triple negative breast cancer

Designing Fit-for-Purpose ADC Candidates

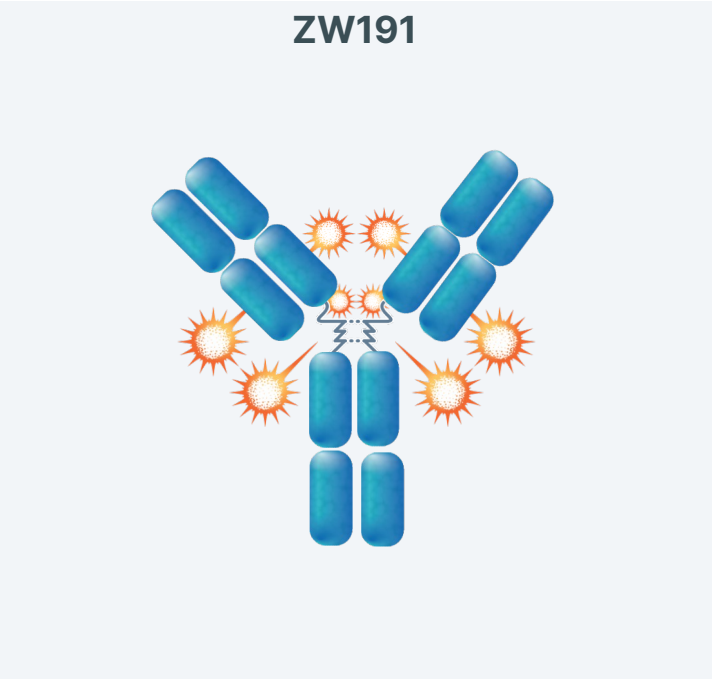
	Zymeworks Strategy Today	Zymeworks Strategy Tomorrow
Target	Focus on targets with evidence of clinical activity in indications of unmet need	Explore novel targets
Antibody	Develop optimal ADC antibodies	Leverage bispecific and biparatopic expertise to develop optimal ADC antibodies
Linker/ Conjugation	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 Preclinical Product Candidate



Target

Folate receptor alpha (FRα, FOLR1) is a clinically validated ADC target

FRα 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 ≥ 30 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

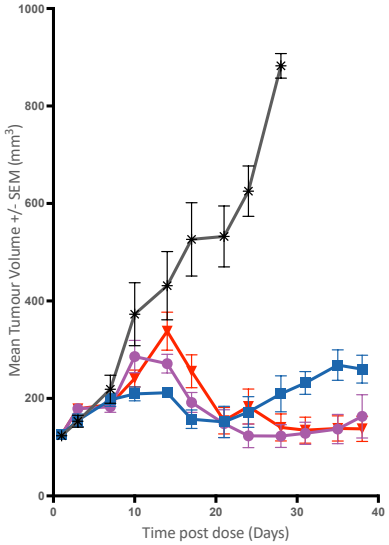
Targeting 2024 IND

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

ZW191 Demonstrates Strong Anti-Tumor Activity in FRα-Expressing Models

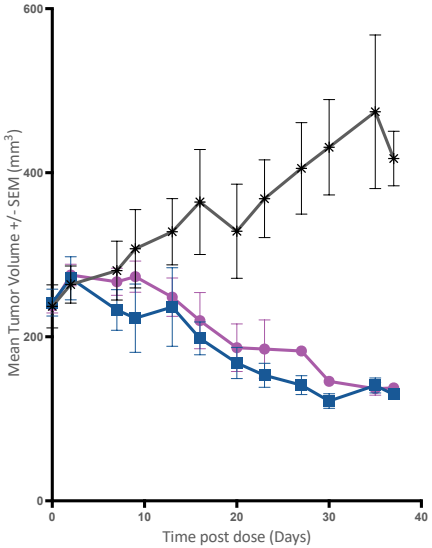
Equivalent Anti-Tumor Activity in FRα-High Expressing Xenograft Models

OV90 Ovarian Carcinoma CDX



ADCs dosed at 6 mg/kg

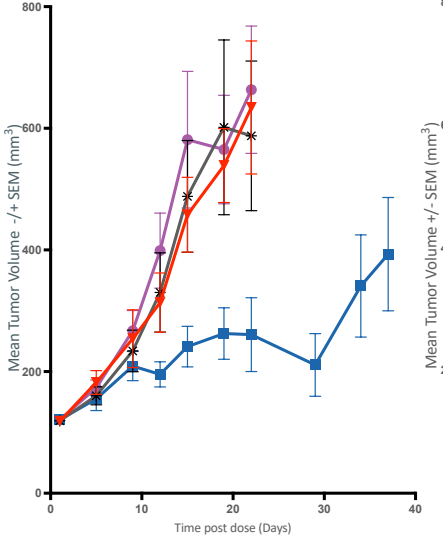
CTG-2025 Ovarian Cancer PDX



ADCs dosed at 6 mg/kg

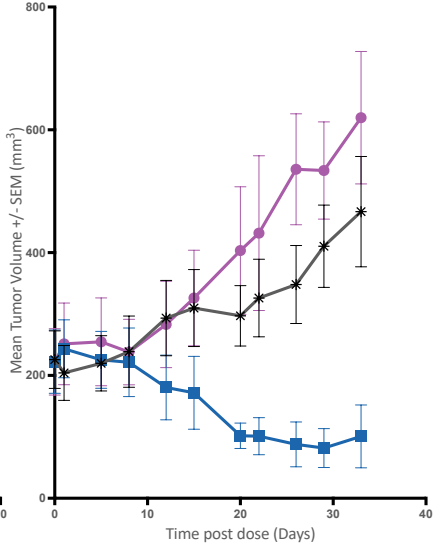
Superior Anti-Tumor Activity in FRα-Mid Expressing Xenograft Models

OVCAR-3 Ovarian Cancer CDX



ADCs dosed at 0.75 mg/kg

CTG-0958 Ovarian Cancer PDX



ADCs dosed at 6 mg/kg

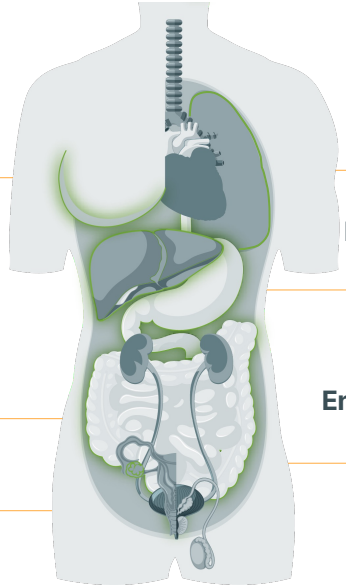
Vehicle ZW191 MORAb-202 Mirvetuximab Soravtansine

ADCs: antibody drug conjugates; CDX: cell line-derived xenograft; FRα: folate receptor alpha; PDX patient-derived xenograft

ZW191 Treatment Opportunity

Potential best-in-class opportunity in FRα-high ovarian cancer
Potential first- and best-in-class in FRα-high endometrial, NSCLC, TNBC, and FRα-mid/low solid tumors

FOLATE RECEPTOR ALPHA EXPRESSING CANCERS



Breast 40-50%

Lung 14-74%

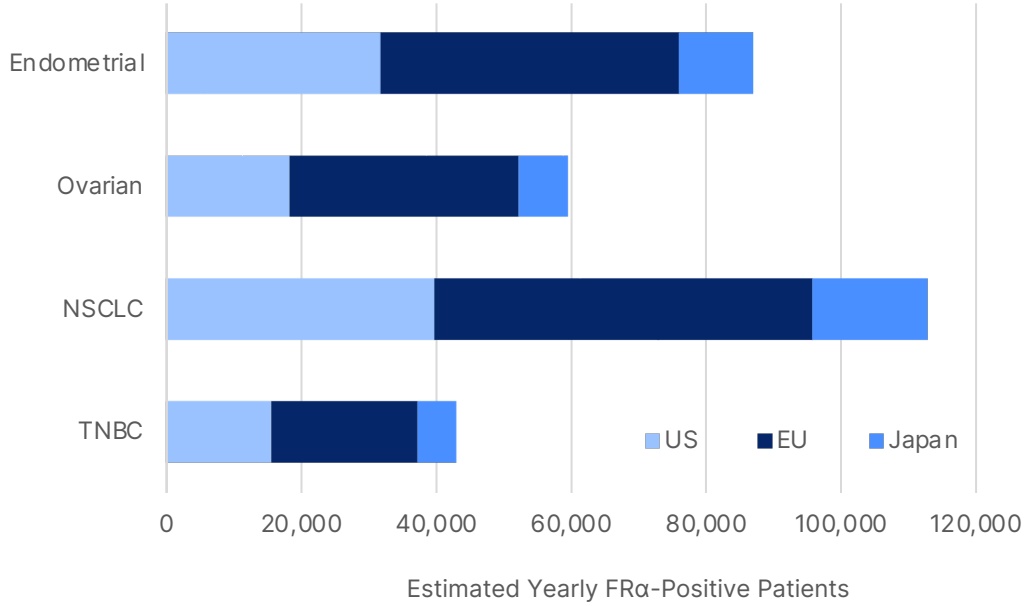
Pancreatic 37%

Ovarian 39-75%

Endometrial 50%

Colorectal 5-25%

ESTIMATE OF NEWLY-DIAGNOSED FRα+ PATIENTS IN KEY INDICATIONS



Expression levels cited from multiple sources including: Senol S et al 2015; Ayada et al. Med Mol Morphol 2018; Oza AM SGO 2021; O'Shannessy DJ et al Oncotarget 2012; Nunez MI et al 2012; D'Angelica et al. Mod Path 2011; Nature Review: Clinical Oncology; Vol. 17 June 2020.

Zymeworks Moving Forward “5 by 5”

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

2017-2022

- Select Product Pipeline
- Platform Technologies & Tools

2022-2027

- **Accelerate Product Pipeline**
- **5 New Molecules in Clinic in 5 Years**
- **Select Product Partnerships**

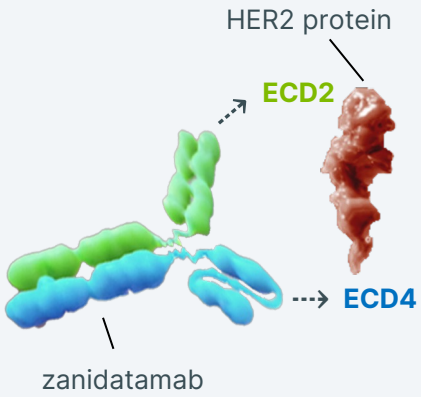
ZANIDATAMAB

Commercial Collaborations

Transactions allow zanidatamab 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

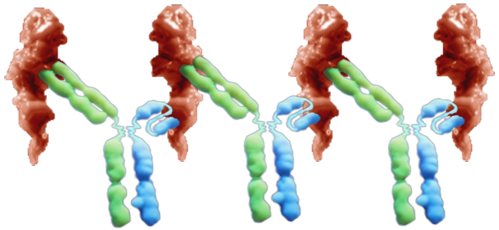
Zanidatamab



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 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

[1] 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

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

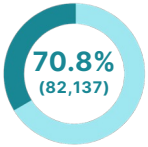
Epidemiology of Biliary Tract Cancer

Biliary Tract Cancers (BTC) are molecularly diverse tumours which include gallbladder cancer (GBC), intrahepatic cholangiocarcinoma (IHCC), and extrahepatic cholangiocarcinoma (EHCC)[1]. Gall bladder cancer is 80-95% of biliary tract cancer cases[2]

Epidemiology (World)

Incidence varies globally:

- GBC accounts for 0.6% of all adult cancers worldwide (~116,000 new cases in 2020)[3,4]
- In 2017, by country, Chile had the highest BTC incidence worldwide, followed by Japan and South Korea (10.83, 8.88, and 8.55/100,000, respectively)[5]
- ~10% of all estimated new gallbladder cancer cases (12,570) occurred in Europe in 2020[4]



of all estimated new gallbladder cancer cases occurred in Asia in 2020[4]

Epidemiology (United States)

Most cases are diagnosed at an advanced stage:

- ~7,500 new cases of BTC diagnosed annually in the US[8]

CASES BY STAGE AT DIAGNOSIS[6,7]

Progression

Second Line:

- 15-44% of patients receive 2L treatment in Western trials; 75-82% receive 2L in Japan trials[9,10]
- 2L chemotherapy yields response rates of < 10%; median overall survival of patients is often < 6 months[11] with a recent phase II trial reporting 8.6 months[12]
- ~40-60% of BTC patients present possible targetable alterations with differences between anatomical subgroups[6,13]

19% of GBC
17% of EHCC
5% of IHCC

Overexpress HER2[14]

2L, second line; HER2, human epidermal growth factor receptor 2;
1.Bogenberger JM et al., Precision Oncol. 2018; 2.Lazcano-Ponce EC et al., CA: Cancer J Clin. 2001; 3.GLOBOCAN. Gallbladder fact sheet. 2020. 4.GlOBOCAN. World fact sheets. 2020; 5.Zhang Y et al., Cancer Epidemiology. 2021; 6.Gómez-España MA, et al., Clin Transl Oncol. 2021; 7.Banales JM et al., Nat Rev Gastroenterol Hepatol. 2020; 8.NCI. SEER. SEER*Explorer: Pancreatic & Biliary Cancer. 2021; 9.Chiang N-J et al., Biomolecules. 2021; 10. Fornaro L et al., Br J Cancer. 2014; 11.Lamarca A et al., J Clin Oncol. 2019; 12.Yoo C et al., Final results *(NIFTY)* abstract 55P presented at ESMO Congress 2022; 13.Bridgewater JA et al., Am Soc Clin Oncol Educ Book. 2016; 14.Galdy S et al., Cancer Metastasis Rev. 2017

Targeted Treatment Options are Rapidly Evolving in Biliary Tract Cancer

Actionable driver mutations have been identified and are generally mutually exclusive from one another (including FGFR pathway, IDH1, BRAF, NTRK, ERBB2 (HER2) MSI-high or MMR deficiency)[9]

Advanced / Metastatic Biliary Tract Cancer

FIRST-LINE TREATMENT OPTIONS

SOC based on ABC-02 trial (Global):
Gemcitabine + Cisplatin
mPFS = 8.4 months, mOS = 11.7months[1]

SOC option with TOPAZ-1 trial (United States):
Cisplatin + Gemcitabine + Durvalumab
mPFS= 7.2months, mOS = 12.9 months[2]

Progression in Metastatic Biliary Tract Cancer

SECOND-LINE TREATMENT OPTIONS

SOC based on ABC-06 trial (Global):
FOLFOX mPFS= 4.0months, mOS = 6.2months[3]

Is Targeted Treatment More Effective Than Chemotherapy?

FGFR2 fusions or rearrangements mPFS = 7.0 months, mOS = 17.5 months[4]
IDH1 mutation, mPFS = 2.7 months, mOS = 10.3 months[5]

Results from HER2 Targeting Agents in 2L+ Trials*

Trastuzumab + FOLFOX mPFS = 5.1months, mOS = 10.7 months[6]
TDXd (HERB trial) mPFS = 5.1months, mOS = 7.1 months[7]
Trastuzumab + Pertuzumab (MyPathway) mPFS = 4.0, mOS = 10.9 months[8]

1L, first line treatment; 2L, second line treatment; BRAF, activating serine/threonine-protein kinase B-raf kinase; ERBB2, receptor tyrosine-protein kinase erB-2; FGFR2, fibroblast growth factor receptor 2; FOLFOX, folinic acid, fluorouracil, and oxaliplatin; HER2, human epidermal growth factor receptor 2; IDH1, isocitrate dehydrogenase 1; MMR, mismatch repair; mPFS, median progression-free survival; mOS, median overall survival; MSI, microsatellite instability; NTRK, neurotrophic receptor tyrosine kinase; SOC, standard of care; TDXd, trastuzumab deruxtecan . * have not received FDA (or any regulatory authority) approval for BTC 2L indication

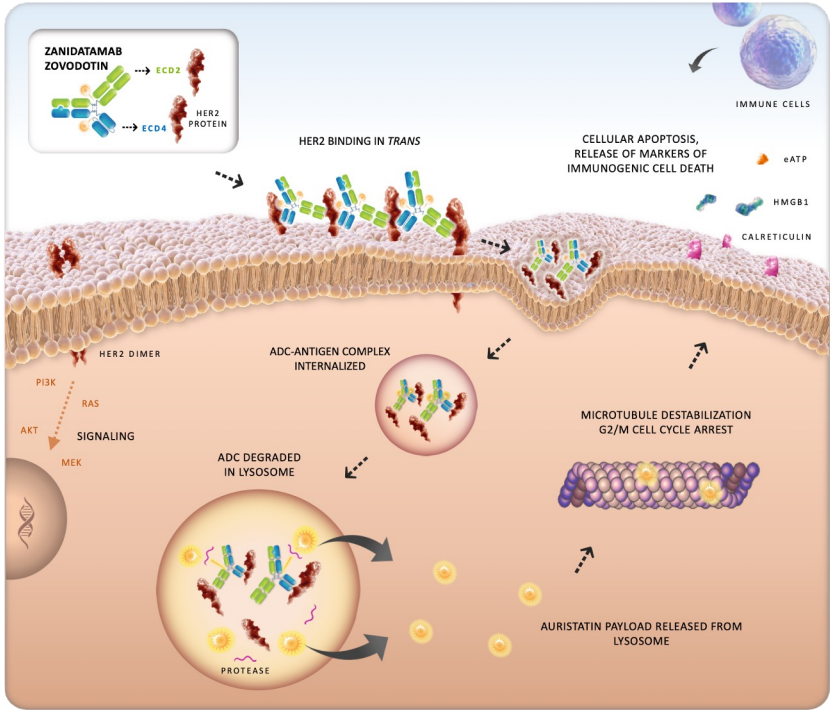
ZANIDATAMAB ZOVODOTIN

Clinical Development

Zanidatamab 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 kinase; PI3K, phosphatidylinositol 3-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

Zanidatamab 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

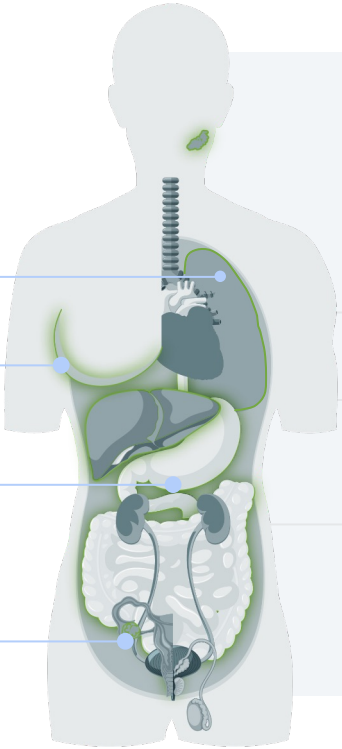
Non-Small Cell Lung Cancer (NSCLC)
HER2-amplified NSCLC

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

Zanidatamab Zovodotin: A Bispecific ADC for HER2-Targeted Therapy

Data Highlights and Catalysts

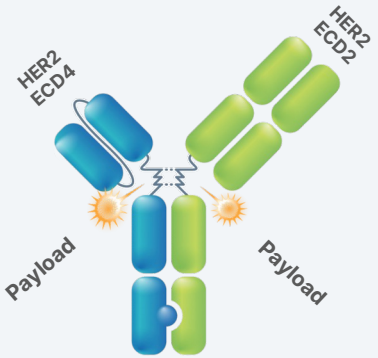
Clinical Data Highlights

- 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 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			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
JNJ-78306358 CD3 x HLA-G Bispecific Azymetric | EFECT	Solid Tumors			Johnson & Johnson Innovation
ATRC-301 EphA2 Targeting ADC 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			LEO
Bispecific Antibody Azymetric | EFECT	Undisclosed			BeiGene

Over $180MM[3] in milestones received to-date

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

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 million[1]

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 resources[2]
- Ongoing funding from Jazz for zanidatamab development[3]
- 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 is unaudited as of 12/31/2022 and excludes approximately $30 million from zanidatamab related reimbursements for R&D expenses incurred in 4Q22

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

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

Future product pipeline and R&D engine

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

Improved financial position provides ability to **rapidly advance** product candidates with a **focus** on next-generation ADC and multispecific technologies

Enterprise Value Framework

Driving value from all five key areas of focus

Strategic priorities underpinned by **experienced management team, improved financial position** with cash runway through at least 2026, and **portfolio** of existing partnership and collaborations

Experienced and Accomplished Leadership Team

Ken Galbraith
Chair & Chief Executive Officer

Neil Klompas, CPA, CA
Chief Operating Officer

Paul Moore Ph.D.
Chief Scientific Officer

Chris Astle, Ph.D.
SVP and Chief Financial Officer

Mark Hollywood
Executive VP and Head of Technical and Manufacturing Operations

Daniel Dex, JD
SVP Corporate Secretary and General Counsel

Jeffrey Smith, M.D.
SVP, Early-Stage Development

Kaycia Wilde, Ph.D.
VP, Clinical Operations

John Fann, Ph.D.
VP, Technical Operations and Process Science

Milan Mangeshkar, Ph.D.
VP, Biometrics

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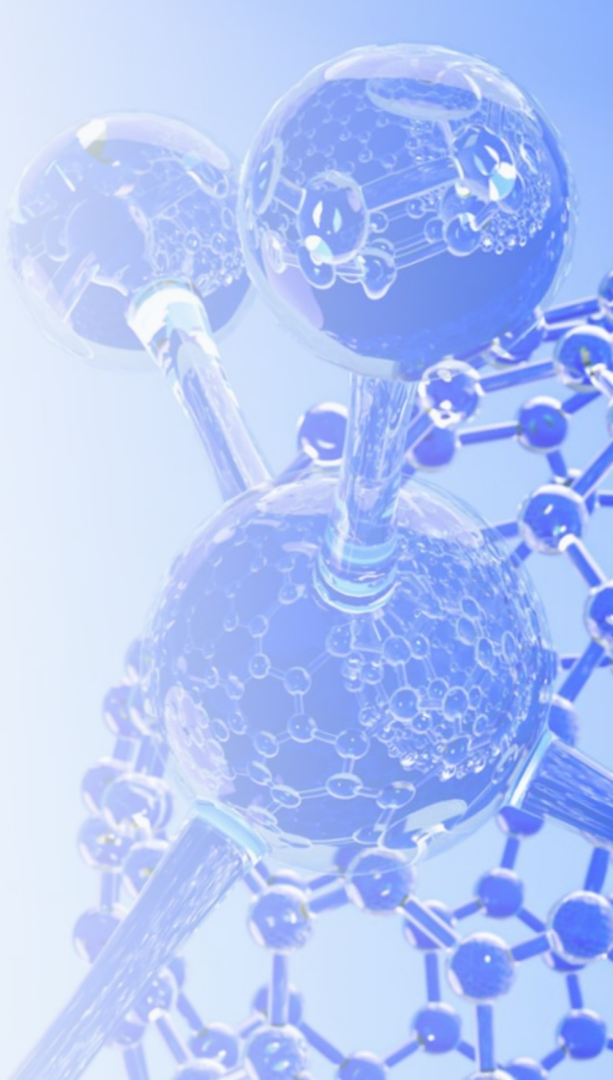


Appendix

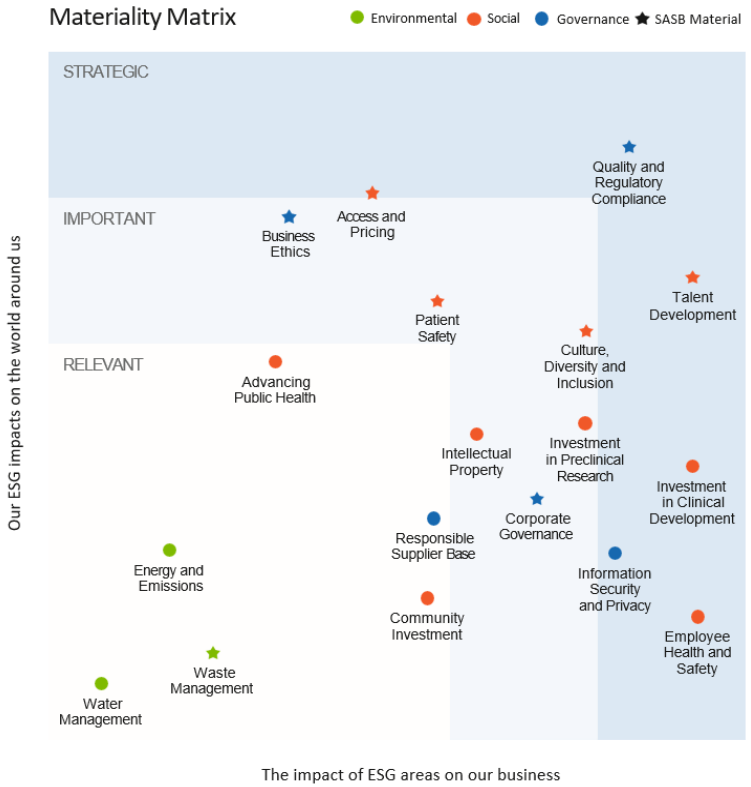
Key Focus Areas

- Talent Development
- Diversity, Equity and Inclusion
- Quality and Regulatory Compliance
- Investment in Clinical Development
- Access and Pricing

Monitoring our key focus areas enable us to understand our key risks and opportunities and focus resources to manage and drive performance in those areas.

As we grow, we will continue to reassess our key focus areas and adjust our strategy and resource allocation to ensure appropriate focus on mitigating risks and seizing opportunities.

We will align our reporting with ESG reporting standards such as IFRS's sustainability standards (ISSB), once they have been finalized. In the future we aim to undertake a full external stakeholder assessment to ensure our strategy and reporting continues to align with the concerns and needs of our stakeholders.



The phrase "materiality" as used in the context of this report is different than the definition used in the context of our filings with the US Securities and Exchange Commission (SEC). Issues deemed material for purposes of this report and for purposes of determining our ESG strategies may not be considered material for SEC reporting purposes.

Zymeworks' Preclinical Assets Show Significant Near-Term Potential

	 ZW171	 ZW191	 ZW251	 ZW220
Target	MSLN x CD3	FRα	GPC3	NaPi2b
Format/ Technology	2 x 1 multispecific/ Azymetric™ heterodimeric Fc	Monospecific/TOPO1i ADC	Monospecific/TOPO1i ADC	Monospecific/TOPO1i ADC
Potential Indications	Ovarian cancer, pancreatic cancer, colorectal cancer	Ovarian cancer, other gynecological cancers, and other solid tumors	Liver cancer	Ovarian cancer, NSCLC
Stage	IND-Enabling	IND-Enabling	Late Discovery	Late Discovery
Next Milestone	**IND 2024**	**IND 2024**	Pilot NHP toxicology study initiated DAR optimization underway	Pilot NHP toxicology study initiated DAR optimization underway

ADC, antibody-drug conjugate; DAR, drug to antibody ratio; Fc: fragment crystallizable region of antibody; NSCLC non-small cell lung cancer; NHP, non-human primate

Zymeworks' Technologies Enable Fit-For-Purpose Design of Multispecifics

TECHNOLOGY	FEATURES	HIGHLIGHTS
Azymetric™ HetFc and HetFab heterodimeric IgG	• Industry-leading heterodimeric IgG solution • Enabling technology for bispecific and multispecific therapeutics • Superior stability, purity and modularity of Azymetric™ allows HTP screening and development of multispecifics	• Clinically validated technology • Multiple pharma partners employing
Biparatopic mAbs	• Enhanced receptor cross-linking via binding of independent epitopes	• Zanidatamab, ZW49
T Cell Engagers (TCE)	• 1+1 T cell engager applications • 2+1 T cell engager engineered to maximize therapeutic window	• JNJ-78306358; JNJ-78278343 (Phase 1) • ZW171 (2024 IND)

TriTCEs
Next Gen trispecific T cell engagers
	• Novel next gen trispecific designed to overcome TCE limitations
	  • TriTCE-costim with potential to re-invigorate 'cold' tumors
	  • TriTCE-CPI (checkpoint inhibition) to overcome suppressive tumor micro-environment
		• Candidate selection ongoing

ProTECT™ Tumor-specific immune stimulation	• Tumor-specific activity via conditional blocking to reduce off-tumor toxicities • Functional block adds checkpoint modulation to enhance efficacy	• Widens scope of possible tumor targets • Interfaces with TriTCE, Antibody or ADC
Cytokine Fc-fusions Tumor-specific cytokine activation	• Novel cytokine engineering approach combining reduced potency and tumor specificity • Can be combined or integrated with other Zymeworks molecules	• Non-core asset: Tumor restricted IL-12 (AACR 2021)

CPI, checkpoint inhibition; HTP, high-throughput screening; MTD, maximum tolerated dose;

Zymeworks' Technologies Enable Fit-For-Purpose Design of ADCs

TECHNOLOGY	FEATURES	HIGHLIGHTS
ZymeLink™ Auristatin Auristatin Drug-linker	• Potent, bystander inactive; induce markers of immunogenic cell death • N-acylsulfonamide spacer links auristatin core to stable cleavable linker; compatible with multiple conjugation strategies • IgG1-like PK and exposure	Used in: • Zanidatamab Zovodotin (ZW49) • XB002 (formerly ICON-2) • ATRC-301
ZymeLink™ Hemiasterlin Hemiasterlin Drug-linker	• Potent, bystander active • N-acylsulfonamide spacer links hemiasterlin core to stable, cleavable linker compatible with multiple conjugation strategies • IgG1-like PK and exposure	• MTD ≥ 15 mg/kg in non-human primates • DAR4 ADC at 15 mg/kg in non-human primates- no evidence of neutropenia or elevations in transaminases
TOPO1i Technology Camptothecin Drug-Linker	• Novel camptothecin payload, bystander active • Stable, cleavable linker compatible with cysteine conjugation • Anti-tumor activity across multiple programs in diverse xenograft models • IgG1-like PK and exposure	• MTD ≥ 30 mg/kg in non-human primates Used in pipeline programs: • ZW191 • ZW220 • ZW251
Site Specific Conjugation Cysteine-Insertion Technology	• Homogeneous conjugation at multiple sites • Combines with Azymetric™, multivalent linkers for precise control of DAR • Sites can mask payload hydrophobicity, protect against metabolism, and limit deconjugation	Used in non-core asset: • cMet-ZLA ADC
TLR7 ISAC Technology Immunostimulatory Drug Conjugate	• Purine-based scaffold using a peptide cleavable linker	• Presented at the Society for Immunotherapy of Cancer (SITC) 2022

CPI, checkpoint inhibition; HTP, high-throughput screening; MTD, maximum tolerated dose;