zymeworks

Making a Meaningful Difference

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

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.

Key Expected R&D Developments in 2024 and 2025

- Initial regulatory submissions by Jazz and BeiGene for potential accelerated approvals for zanidatamab in second-line+ HER2-amplified biliary tract cancers (BTC)
- Topline data readout in 2024 from global pivotal study of zanidatamab in first-line gastroesophageal adenocarcinoma (GEA) HER2+ (HERIZON-GEA-01) to support global regulatory submissions
- Additional clinical studies to be initiated by Jazz and BeiGene for zanidatamab beyond BTC and GEA
- New product candidate nomination to fulfill 5x5 R&D strategy with up to four new INDs filed during 2024 and 2025 (including ZW171, ZW191, ZW220)
- Zanidatamab zovodotin (ZW49) studies ongoing in Phase 2 HER2+ non-small cell lung cancer patients in combination with PD-1 inhibitor
- Initial expansion of R&D efforts into autoimmune disease and inflammation

HER2: human epidermal growth factor receptor 2; IND: investigational new drug

Projected Cash Runway Supports Current Strategy Through 2026 and Potentially Beyond

Updated Financial Guidance:

Cash resources of **$431 MM**
(as of June 30, 2023)

Q2 2023 net operating cash burn of **$30 MM**

Potential sources to extend cash runway:

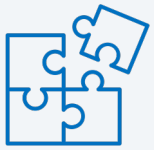
- Royalty income and commercial milestones from zanidatamab sales by Jazz and BeiGene
- Additional payments from legacy technology platform collaborations
- New partnerships/collaborations to provide upfront payments and committed R&D funding

1. Net operating cash burn includes planned capital expenditures of $15MM for 2023
2. Ongoing funding for zanidatamab related development expenses incurred by Zymeworks and reimbursed by Jazz Pharmaceuticals will be recorded as revenues
3. Cash resources for 2Q23 do not include potential reimbursable amounts related to the development of zanidatamab

Multifunctional Antibody Therapeutics for Oncology (and Beyond)

Focus on Cancer Indications with Greatest Unmet Patient Need

Committed to transform current standard of care for patients with poor prognosis
(e.g., lowest 5-year OS)



Integrated R&D Engine

Customized antibodies through in-house protein engineering and proprietary technology

Combinable technology allows for multi-modality solutions with distinct and novel mechanisms of action

Desired Product Profile

First and second-line market opportunities

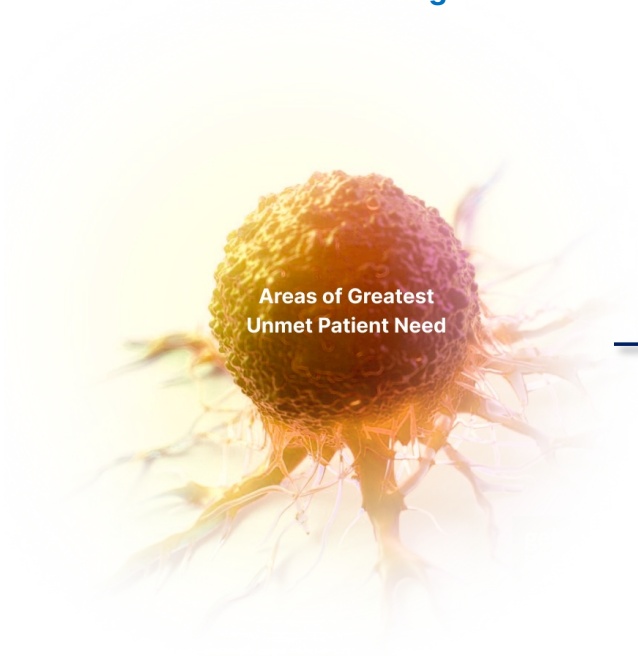
Pursuing lead indications with global peak sales potential >$1 B

Strategy to retain US commercial rights

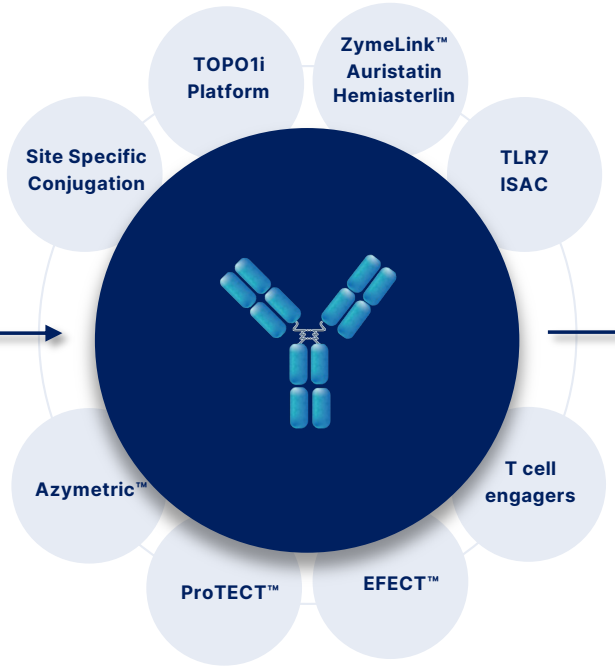
OS: overall survival
1.Combinable proprietary technologies include: Azymetric; EFECT; ProTECT; ADC Platform includes cysteine insertion technology and novel payloads

ADC and Multispecific Modalities Driving Our Pipeline

Select Difficult-to-Treat Cancers & Target

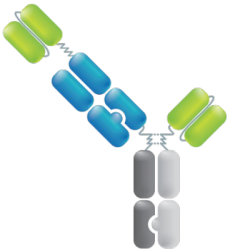


Design with Complementary Technology



Optionality with Two Foundational Fit-for-Purpose Modalities

Antibody Drug Conjugates
Customization:
- Antibody properties
- Antibody format
- Payload
- DAR



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

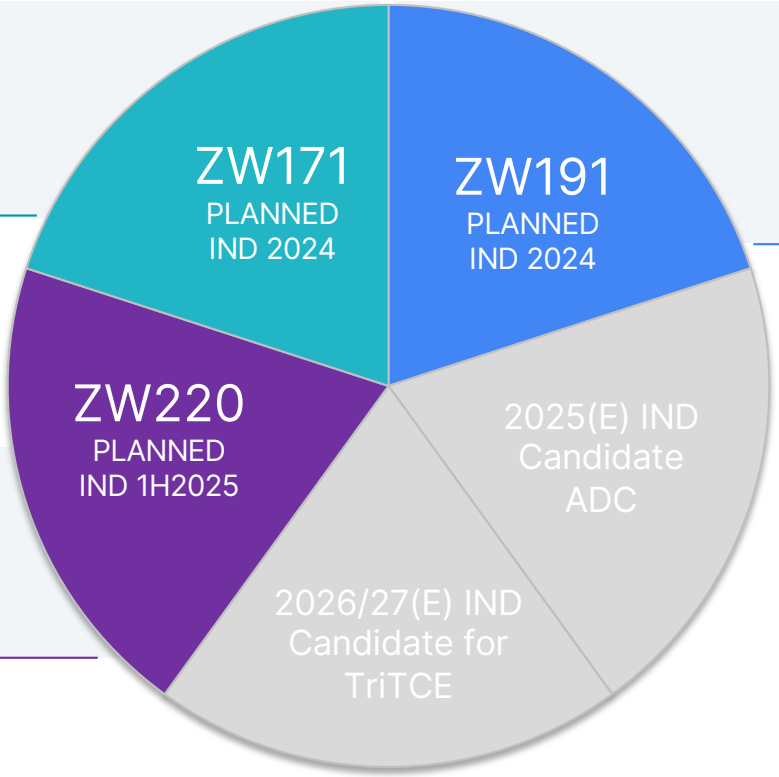
Goal of 5 **New** INDs by 2027

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

"5x5" R&D Strategy: Portfolio Construction

ZW171
Bispecific T-Cell Engager
targeting pancreatic, mesothelioma, ovarian, and other mesothelin-expressing cancers

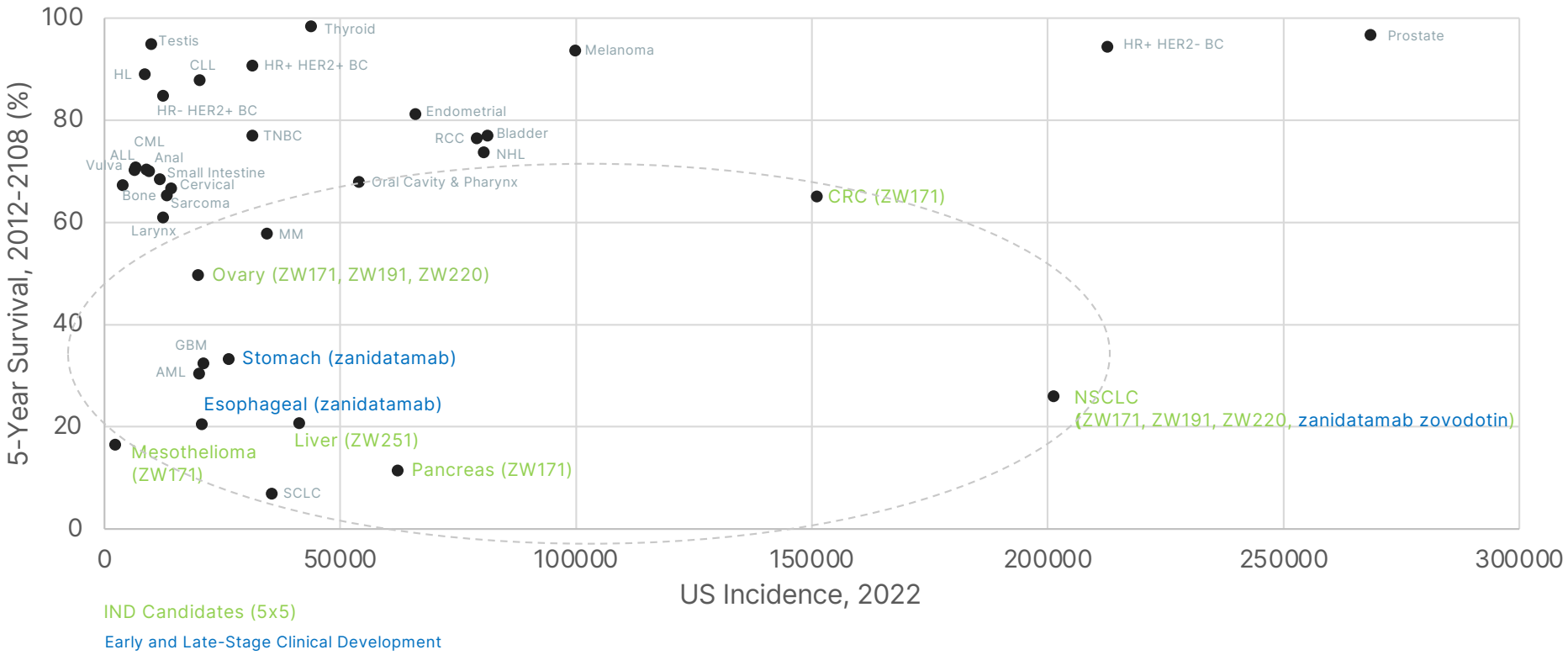
ZW191
Antibody Drug Conjugate
targeting folate receptor alpha expressing tumors including ovarian, other gynecological, and non-small cell lung cancers



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

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

Focus on Cancers With Highest Unmet Medical Need



SEER*Explorer, accessed 10 Oct 2022

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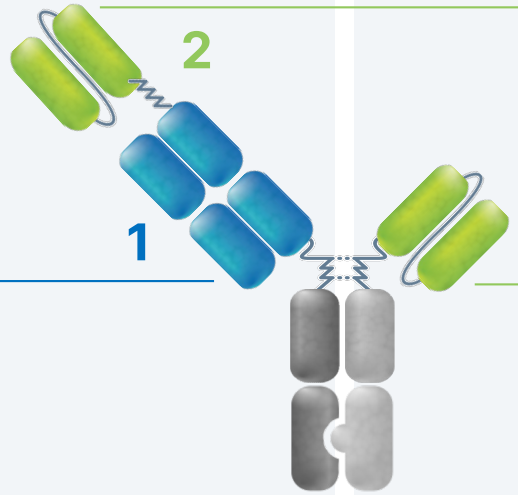
Multispecific Antibody Therapeutic (MSAT) Program

Multispecific Antibody Therapeutics Development

Engineering and Optimizing the Design of T Cell Engagers is Not Trivial

Anti-CD3 paratope
- Affinity
- Epitope
- Stability
- Format

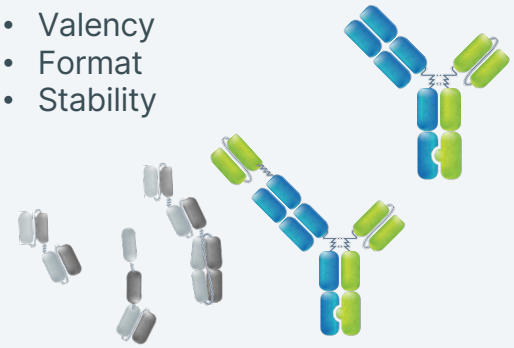


e.g., ZW171

Anti-TAA paratope
- Affinity
- Epitope
- Valency
- Stability
- Format

3

Antibody Format and Geometry
- Half life
- Valency
- Format
- Stability

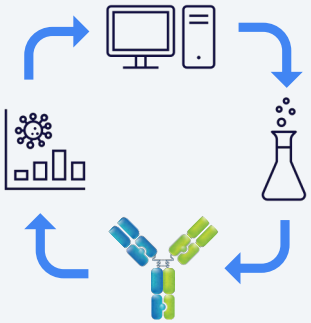


T cell engager antibody design is critical for a **widened therapeutic index** and **optimal T cell synapse formation**

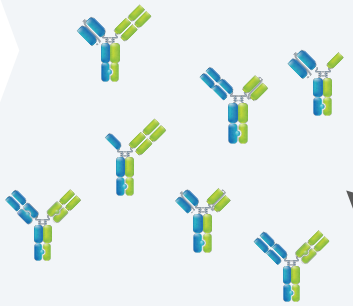
TAA: tumor associated antigen; TCE: t cell engager

Core Competency of Protein Engineering & Flexibility of Azymetric™ Platform Enables Screening of Multiple Parameters in Parallel

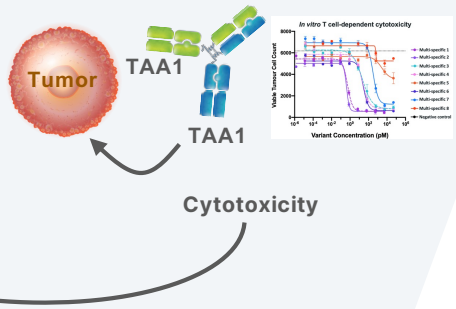
Paratope screening & optimization, *in silico* affinity engineering



Generate panel of extensively engineered antibodies: valency, geometry & affinity



In vitro & *in vivo* biophysical and functional characterization of multispecific antibodies



Single lead optimized to:

- Target TAA over-expressing cells
- Improve T cell responses
- Maximize therapeutic index
- Modulate cytokine release

- Core competency of protein engineering harnessed to engineer and optimize multiple parameters in silico
- Flexibility of Azymetric™ platform enabled extensive screening of antibodies based on valency, geometry, and affinity

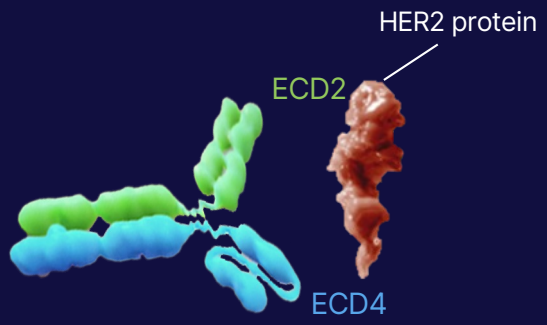
TAA: tumor associated antigen

Differentiated Development of Multi-Specific Antibody Therapeutics

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

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

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



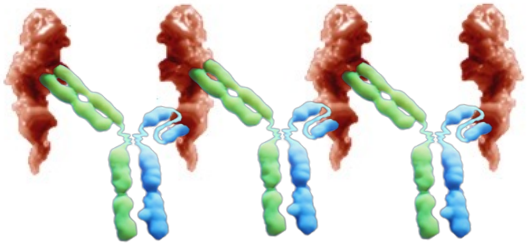
Zanidatamab

A Bispecific Antibody for HER2-Expressing Cancers

Zanidatamab's Unique Format Promotes:

- Ability to target two distinct HER2 epitopes and results in HER2 binding across a range of expression levels (low to high)[1]
- HER2-receptor cross-linking, enhanced receptor clustering, internalization, and receptor downregulation[1]
- Inhibition of cellular proliferation
- Fc-mediated cytotoxicity: ADCC, ADCP, CDC[1]

Biparatopic HER2-Binding of Zanidatamab Drives Multiple Mechanisms of Action



The geometry of zanidatamab prevents it from binding to the same HER2 molecule[1]

Note: Zanidatamab was granted Breakthrough Therapy designation by the FDA for patients with previously-treated HER2 gene-amplified biliary tract cancer (BTC) as well as two Fast Track designations, one for previously treated or recurrent HER2-positive BTC and another for first-line gastroesophageal adenocarcinoma (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 from the European Medicines Agency. Zanidatamab was granted Break Through designation from the Center of Drug Evaluation in China for patients with BTC who have failed prior systemic therapies.

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

1.Weisser N et al., Nature Communications 2023

Proven Engineering: Zanidatamab - A HER2 Bispecific Antibody Currently in Clinical Trials

Clinical Data

Differentiated tolerability profile amongst HER2-targeted therapies; majority of adverse events low grade

Single Agent Activity in Second-Line BTC

- 41.3% ORR, 12.9 months mDoR[1]

Combination Activity in First-Line GEA

- 79% ORR, 20.4 months mDOR, 84% 18 month OS rate[2]
- Update on Phase 2 first-line GEA trial to be presented at ESMO 2023[3]

Pivotal Trials

HERIZON-BTC-01
A Global Pivotal Study in Second-Line HER2-Amplified BTC

Results presented at ASCO 2023 with concurrent publication in The Lancet Oncology[1]

HERIZON-GEA-01
A Global Pivotal Study in First-Line HER2-Positive GEA[4]

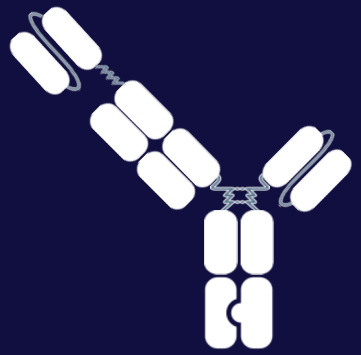
Supported by promising Phase 2 survival data presented at ASCO GI 2022[2]

Expected Catalysts

- Planning for potential accelerated approval of zanidatamab in second-line BTC, Jazz has alignment with FDA on confirmatory trial in first-line metastatic BTC
- Topline data for the Phase 3 HERIZON-GEA-01 trial expected in 2024
- Clinical data generation continues across HER2-expressing cancers including early-stage breast cancer

Collaboration Partners:

BTC: biliary tract cancers; GEA: gastroesophageal adenocarcinoma; HER2: human epidermal growth factor receptor 2; mDOR: median duration of response; ORR: overall response rate; OS overall survival
1. Harding et al., Lancet Onco 2023 2. Elimova E et al., Abstract #347 presented at ASCO GI 2022, JCO 41(4S) 3. NCT04276493 4. NCT05152147



ZW171
MSLN x CD3 Multispecific

A bispecific T-cell engager on track for IND filing in 2024

Design
Optimized 2+1 avidity driven geometry incorporating novel low affinity CD3 binder to direct T-cell targeting of MSLN expressing tumors

Mechanism
Engages immune system via MSLN-dependent T-cell activation to direct efficient tumor killing with limited cytokine release

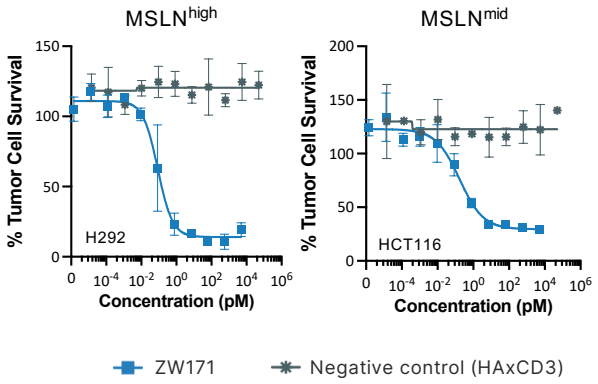
Profile
Enhanced anti-tumor activity and safety profile in preclinical models supports opportunity to overcome clinical limitations of prior MSLN-directed therapies

IND: investigational new drug; MSLN: mesothelin; scFV: single-chain variable fragment
1. Afacan N et al., Abstract #2942 presented at AACR 2023

ZW171: MSLN x CD3 T-Cell Engaging Multispecific

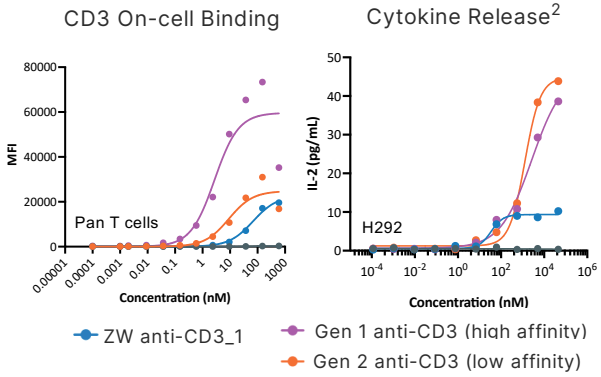
Engineered with 2+1 Format
Facilitates Avidity-Driven Binding[1]

Tumor Cell Cytotoxicity in Mid–to-High Expressing MSLN Models[1]



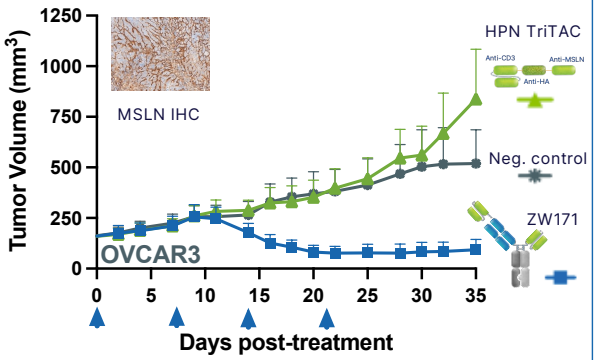
Novel CD3 Paratope with Enhanced Safety

Proprietary CD3 engager has low affinity CD3 binding and cytokine release[1]



Pilot NHP toxicology data shows ZW171 is well-tolerated up to 30 mg/kg[1]

Differentiated by Greater Anti-Tumor Activity
in MSLN-Expressing Tumor Models[1]



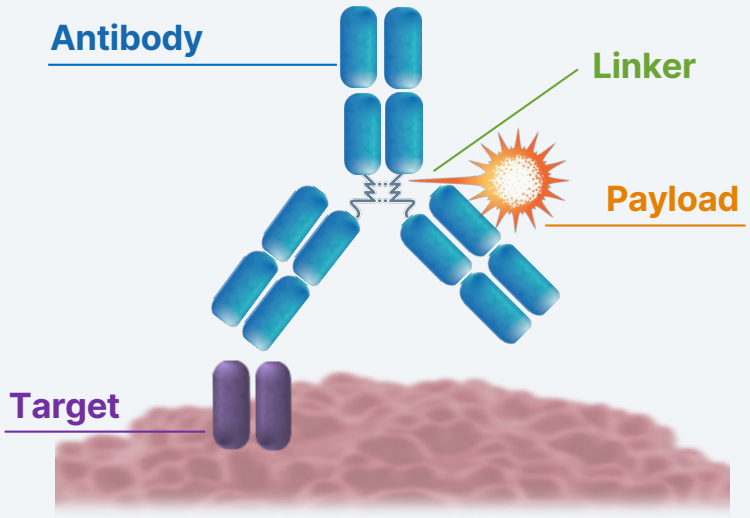
OVCAR-3 tumor engrafted mice were humanized with donor PBMC (3 donors) and dosed i.v. QW x4 with ZW171 or i.p. daily x 18 with HPN triTAC.
Neg control (HAxCD3)

bsAb: bispecific antibody; Gen: generation; MSLN: mesothelin
1. Afacan N et al., Abstract #2942 presented at AACR 2023 2. Cytokine release from T cell dependent cytotoxicity assay with pan T cells and H292 tumor cells at 5:1 E:T

Antibody-Drug Conjugate (ADC) Program

Building Next-Generation ADCs

Next-Generation ADCs



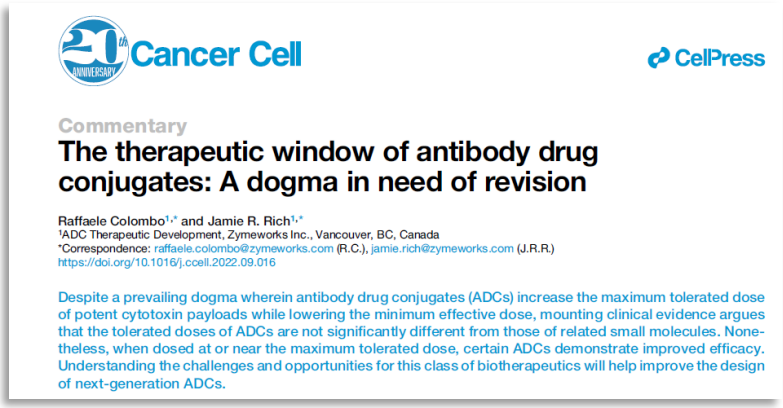
- Focusing on **validated targets** provides opportunity for benchmarking in preclinical development and expected clinical differentiation; novelty of targets anticipated to increase over time
- Exploiting our **proprietary TOPO1i payload (ZD06519)** while exploring alternate mechanisms of action for longer-term development
- Leveraging validated **peptide-cleavable linkers** and **stochastic conjugation**. New chemistries under development to complement novel payloads
- Optimizing **antibody properties** for the ADC mechanism. Biparatopic and bispecific ADC formats may also provide future differentiated therapeutics

Multiple Topoisomerase 1 inhibitor ADCs[1,2] **advancing towards the clinic** with **broad investment in ADC technologies to support future programs**

ADC: antibody drug conjugate; TOPO1i: topoisomerase 1 inhibitor

1. Colombo R, Rich JR. Cancer Cell 2022 (40)
2. Colombo R, Barnscher SD, Rich, JR. Cancer Res 2023, *83* (7). Abstract #1538 presented at AACR 2023

Platform Design Criteria Draw on Well Validated ADC Technologies



Cancer Cell

CellPress

Commentary

The therapeutic window of antibody drug conjugates: A dogma in need of revision

Raffaele Colombo[1,*] and Jamie R. Rich[1,*]
[1]ADC Therapeutic Development, Zymeworks Inc., Vancouver, BC, Canada
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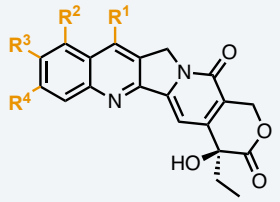
https://doi.org/10.1016/j.ccell.2022.09.016

Despite a prevailing dogma wherein antibody drug conjugates (ADCs) increase the maximum tolerated dose of potent cytotoxin payloads while lowering the minimum effective dose, mounting clinical evidence argues that the tolerated doses of ADCs are not significantly different from those of related small molecules. Nonetheless, when dosed at or near the maximum tolerated dose, certain ADCs demonstrate improved efficacy. Understanding the challenges and opportunities for this class of biotherapeutics will help improve the design of next-generation ADCs.

Payload

Novel camptothecin with moderate potency and strong bystander activity

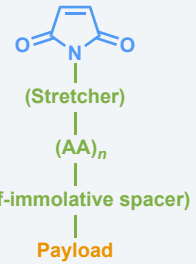
- Acknowledges complex mechanisms driving TOPO1i ADC action
- Sufficient tolerability to achieve ADC dose > 5 mg/kg



Linker

Traceless, plasma-stable, cleavable peptide

- Common to majority of approved ADCs
- Compatible with desired bystander activity
- Avoids highly stabilized linker-antibody conjugation to limit off target toxicities



Conjugation

Thiol-maleimide chemistry

- Stochastic conjugation utilized in all approved ADCs
- Facilitates DAR optimization
- Good balance of stability, safety, and anti-tumor activity

ADC: antibody drug conjugate; DAR: drug to antibody ratio; TOPO1i: topoisomerase 1 inhibitor

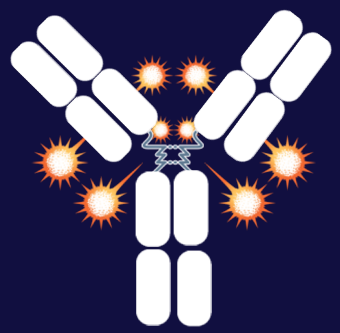
Differentiated Development of Antibody Drug Conjugates

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

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

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

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



ZW191
FRα-targeting ADC

On track for IND filing in 2024

Design
Antibody selected for enhanced internalization and tumor penetration paired with a novel bystander active topoisomerase 1 inhibitor payload (ZD06519) with a DAR8 configuration[1]

Mechanism
Delivery of novel bystander active topoisomerase 1 inhibitor payload (ZD06519) to FRα expressing tumors

Profile
Differentiated efficacy in preclinical tumor models and favorable safety profile supports opportunity to treat broader range of FRα-expressing cancers[1*]

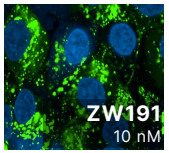
*Gyne; NSCLC; TNBC;
ADC: antibody drug conjugate; DAR: drug to antibody ratio; FRα: folate receptor alpha; IND: investigational new drug

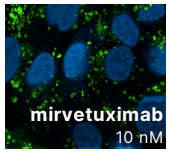
1. Lawn S et al. Abstract # 2641 Presented at AACR 2023

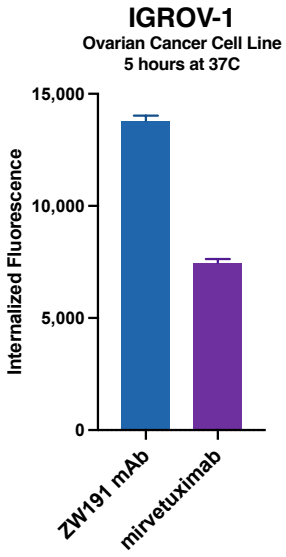
On Track for Clinical Studies in 2024: ZW191 FRα ADC

Customized format for enhanced function

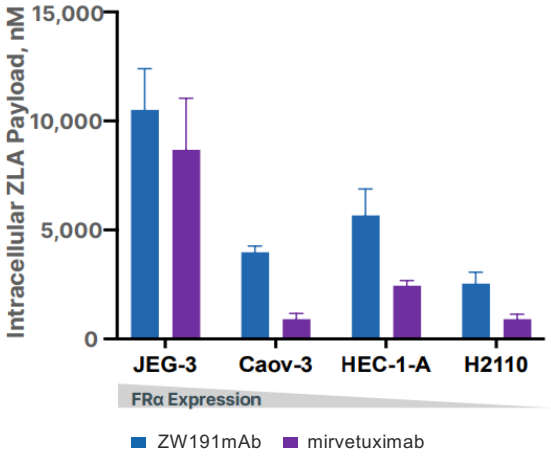
Selected for Enhanced Internalization





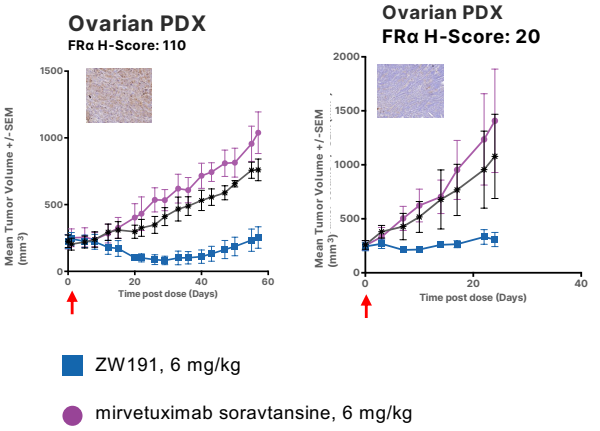


Optimized for Superior Payload Delivery



Differentiated by Greater Anti-Tumor Activity

Anti-tumor activity of ZW191 and mirvetuximab soravtansine against ovarian patient derived xenografts (PDXs) expressing moderate and low FRα



ADC: antibody drug conjugate; FR α: folate receptor alpha; mAb monoclonal antibody
Lawn S et al. Abstract # 2641 Presented at AACR 2023

ZW220
NaPi2b-targeting ADC

On track for IND filing in 1H-2025

Design
An ADC antibody selected for its strong binding and internalization, conjugated in a DAR4 configuration[1]

Mechanism
Delivery of a novel, bystander active topoisomerase 1 inhibitor (ZD06519)[1]

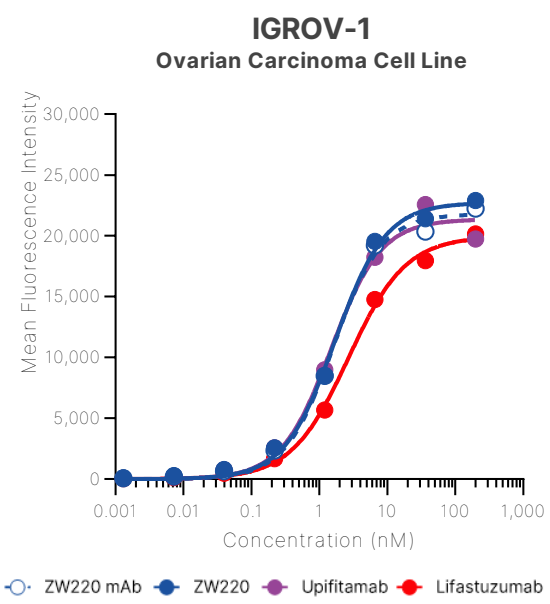
Profile
A NaPi2b ADC demonstrating activity across preclinical tumor models,[1] with first-in-class potential in ovarian and non-small cell lung cancer

ADC; antibody drug conjugate; DAR: drug to antibody ratio; IND: investigational new drug; NaPi2b: sodium-dependent phosphate transporter
1. Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023

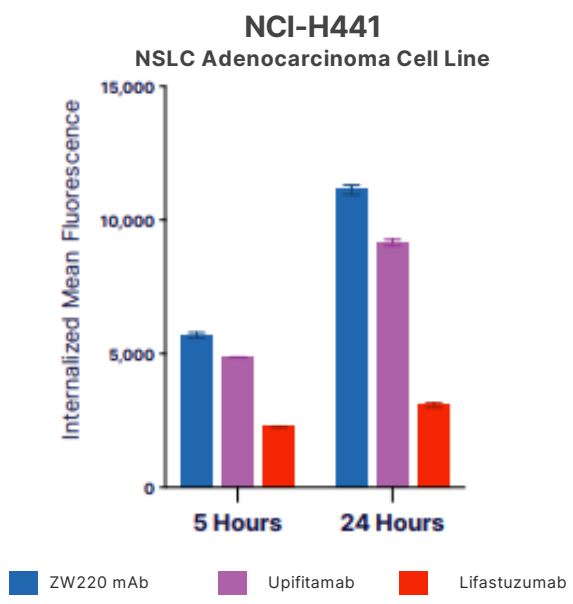
On Track for Clinical Studies in 2025: ZW220 NaPi2b-targeting ADC

Customized format for function with best-in-class and first-in-class potential

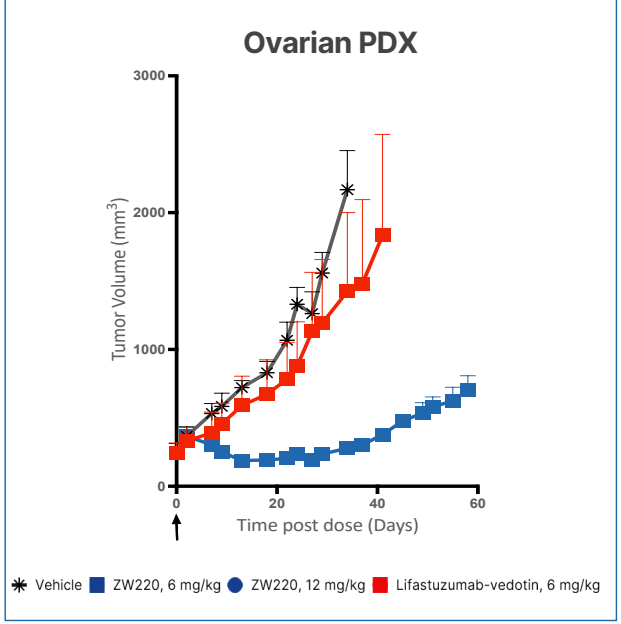
Selected for Strong Binding



Efficient Internalization Drives Payload Delivery



Differentiated Activity in Tumor PDX Models



NaPi2b: sodium-dependent phosphate transporter; nM: nanomolar; mAb: monoclonal antibody; NSCLC: non-small cell lung cancer; PDX: patient derived xenograft
Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023

ZW251
Glypican 3-targeting ADC

GPC3 is expressed in 76% of hepatocellular carcinomas (HCC) and exhibits limited expression in healthy tissues, with high expression observed in ~55% of HCC[1]

Design
An antibody selected for optimal ADC characteristics, including strong binding and internalization, paired with a topoisomerase 1 inhibitor payload (ZD06519)

Mechanism
Delivery of a novel, bystander active topoisomerase 1 inhibitor (ZD06519)[2]

Profile
A GPC3 ADC for HCC with first in class potential and a novel payload demonstrating activity across models[2]

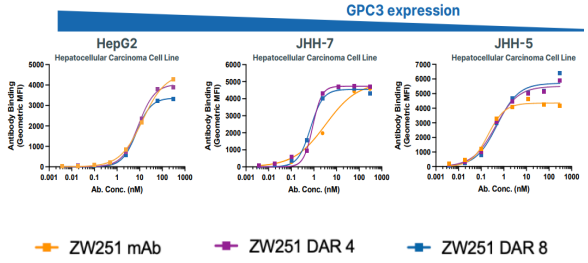
ADC: antibody drug conjugate; DAR: drug to antibody ratio; GPC3: glypican-3; HCC: hepatocellular carcinoma
1. Wang HL et al., Arch Pathol Lab Med 2008 2.Madera L et al., Abstract #2658 presented at AACR 2023

GPC3-Targeting ADC for Hepatocellular Carcinoma

Evaluating optimal design

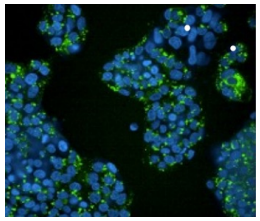
Selected for Strong Binding Across a Range of Expression Levels

Binding of ZW251 mAb and ADC to cancer cell lines across a range of GPC3 expression

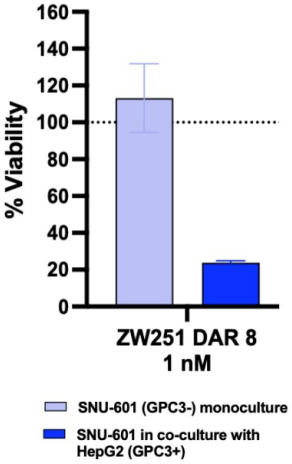


Optimized Internalization of ZW251 with Bystander Activity in Cancer Cell Co-Culture Assay

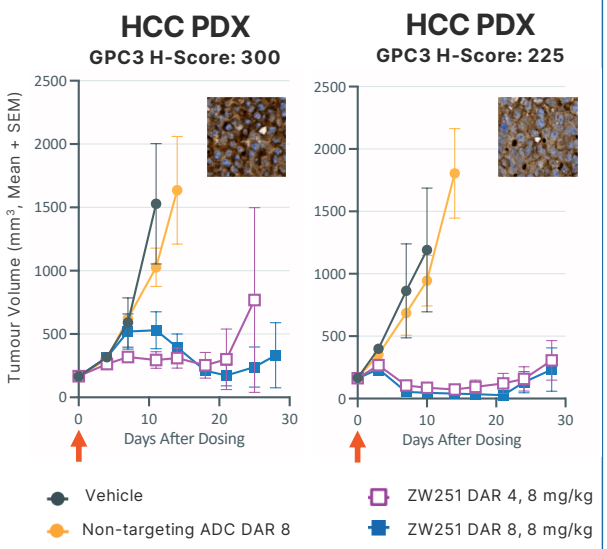
ZW251 internalized in HepG2 cell line



ZW251 Bystander Activity

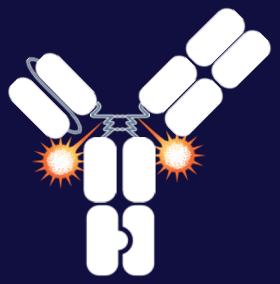


Differentiated Modality Demonstrates Anti-Tumor Activity in HCC models



ADC: antibody drug conjugate; DAR: drug to antibody ratio; GPC3: glypican-3; HCC: hepatocellular carcinoma; mAb; monoclonal antibody; PDX: patient-derived xenograft

1. Madera L et al., Abstract #2658 presented at AACR 2023



Zanidatamab zovodotin

A Bispecific HER2-targeting ADC

Phase 2 expansion into NSCLC in 2023

Design

Novel cross-linking binding enhances internalization of payload and initializes immunogenic cell death

Mechanism

Delivery of novel auristatin payload (ZD02044) covalently linked via a protease cleavable linker in a DAR2 configuration

Profile

Differentiated format offers options to overcome potential points of resistance via geometry and cytotoxin; manageable low-grade adverse events

ADC: antibody drug conjugate; DAR: drug to antibody ratio; ECD: extracellular domain; HER2: human epidermal growth factor receptor 2; NSCLC: non-small cell lung cancer

1.Hamblett, KJ et al., Abstract #3914 presented at AACR 2018; Cancer Res 2018;78(13S) 2.Barnscher S et al., Abstract #2633 presented at AACR 2023 3.Jhaveri K et al., presented at ESMO 2022; #460MO Annals of Oncology 33(7)

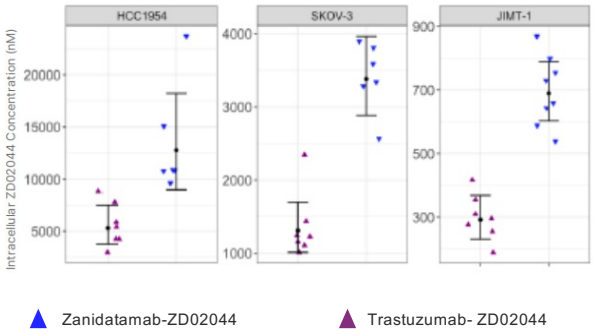
Zanidatamab Zovodotin: A Bispecific HER2-Targeting ADC

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

Engineered for Enhanced Internalization of Payload

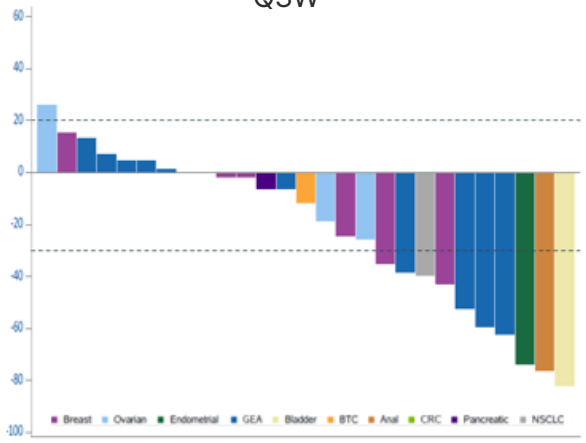
Biparatopic binding elicits internalization, auristatin-mediated cytotoxicity and strong hallmarks of immunogenic cell death[1,2]

Same payload, different backbone = different result



Antitumor Activity Across Solid Tumors

Confirmed ORR of 31%, DCR of 72% in 29 response-evaluable, heavily-pretreated patients at 2.5 mg/kg Q3W[3]



Differentiated Safety Profile

Low grade, manageable ocular adverse events[3]

- MTD not reached
- No ILD or pneumonitis reported
- Any grade keratitis of 43%; all cases decreased to grade 1 or resolved; ocular mitigation program developed
- Any grade alopecia 25%
- Any grade diarrhea 25%

ADC: antibody drug conjugate; DCR: disease control rate; HER2: human epidermal growth factor receptor 2; ILD: Interstitial lung disease; MTD: maximum tolerated dose; ORR overall response rate; Q3W: every three weeks

1.Hamblett, KJ et al., Abstract #3914 presented at AACR 2018; Cancer Res 2018;78(13 Suppl) 2.Barnscher S et al., Abstract #2633 presented at AACR 2023 3.Jhaveri K et al., presented at ESMO 2022; 460MO Annals of Oncology 33(7)

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

R&D Strategy

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

Therapeutic Optionality

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

Financial Structure

Combination of internally-funded and partnered development programs

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

Key Events and Milestones for Remainder of 2023

- **Present updated clinical data on Phase 2 GEA study of zanidatamab + tislelizumab + chemo at ESMO in Madrid in October**
- **Present additional Phase 1 data** for zanidatamab zovodotin (ZW49) at a major medical conference
- Initiate Phase 2 study of zanidatamab zovodotin in combination with PD-1 inhibitor in non-small cell lung cancer
- Present additional preclinical data for pipeline programs at a major scientific conference
- Additional presentations of HERIZON-BTC-01 zanidatamab data by Jazz and BeiGene

ESMO: European society for medical oncology; GEA: gastroesophageal adenocarcinoma; SITC: society for immunotherapy of cancer

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

Differentiated future product pipeline

focused on cancer indications with the greatest unmet patient need and driven by expected progress of zanidatamab zovodotin, ZW171, ZW191, and ZW220

Financial position provides ability to **rapidly advance product candidates focused on transforming the current standard of care** for patients with poor prognosis

Integrated R&D engine from target selection through to pivotal studies

grounded by in-house engineering focused on developing next-generation ADC and multispecific technologies

Complementary therapeutic platforms and fully integrated drug development engine provide the **flexibility and compatibility to precisely engineer and develop highly differentiated antibody-based therapeutics**

Experienced Leadership Team

Ken Galbraith **Chair & Chief Executive Officer**	MacroGenics, AnorMED, Celator Pharmaceuticals, QLT Inc.
Paul Moore Ph.D. **Chief Scientific Officer**	MacroGenics, Celera, Human Genome Sciences
Chris Astle, Ph.D. **SVP and Chief Financial Officer**	Alder BioPharmaceuticals, Allergan, Gilead, pwc
Mark Hollywood **Executive VP and Head of Technical and Manufacturing Operations**	Bristol Myers Squibb, ZymoGenetics, Amgen
Jeffrey Smith, M.D. **SVP, Early-Stage Development**	Alder BioPharmaceuticals, Hoechst, P&G, gsk
Daniel Dex, JD **SVP Corporate Secretary and General Counsel**	Avigilon, mcmillan
John Fann, Ph.D. **VP, Technical Operations and Process Science**	AGC Biologics, Bristol Myers Squibb, abbvie
Josemund Menezes, MBBS **Managing Director, Early-Stage Development (Asia Pacific)**	Aslan Pharmaceuticals, Tessa Therapeutics, Sanofi Pasteur

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