zymeworks

Making a Meaningful Difference

On a mission to improve the standard of care for difficult-to-treat diseases

Investor and Analyst Presentation

JANUARY 11, 2024

Nasdaq: ZYME | zymeworks.com

Legal Disclaimer

This presentation and the accompany oral commentary include “forward-looking statements” or information within the meaning of the applicable securities legislation, including Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements in this presentation and the accompanying oral commentary include, but are not limited to, statements that relate to Zymeworks’ anticipated cash runway and potential sources of its cash runway; preliminary and unaudited estimates of its cash, cash equivalents, and marketable securities; the timing of anticipated IND filings; Zymeworks’ expectations regarding implementation of its strategic priorities; the anticipated benefits of the collaboration agreement with Jazz and BeiGene, including Zymeworks’ ability to receive any future milestone payments and royalties thereunder; the potential addressable market of zanidatamab; the timing of and results of interactions with regulators; Zymeworks’ clinical development of its product candidates and enrollment in its clinical trials; anticipated preclinical and clinical data presentations and publications; expectations regarding future regulatory filings and approvals and the timing thereof; potential therapeutic effects of zanidatamab and Zymeworks’ other product candidates; expected financial performance and future financial position; the commercial potential of technology platforms and product candidates; anticipated continued receipt of revenue from existing and future partners; Zymeworks’ preclinical pipeline; anticipated sufficiency of cash resources and other potential sources of cash to fund Zymeworks’ planned operations through at least the end of H2 2027, and potentially beyond; and Zymeworks’ ability to execute new collaborations and partnerships; and other information that is not historical information. When used herein, words such as “plan”, “believe”, “expect”, “may”, “continue”, “anticipate”, “potential”, “will”, “progress”, and similar expressions, or any discussion of strategy, are intended to identify forward-looking statements. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon Zymeworks’ current expectations and various assumptions, including, without limitation, Zymeworks’ examination of historical operating trends. Zymeworks believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Zymeworks may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various factors, including, without limitation: any of Zymeworks’ or its partners’ product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; Zymeworks may not achieve milestones or receive additional payments under its collaborations; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions; the impact of pandemics and other health crises on Zymeworks’ business, research and clinical development plans and timelines and results of operations, including impact on its clinical trial sites, collaborators, and contractors who act for or on Zymeworks’ behalf; clinical trials may not demonstrate safety and efficacy of any of Zymeworks’ or its collaborators’ product candidates; Zymeworks’ assumptions and estimates regarding its financial condition, future financial performance and estimated cash runway may be incorrect; inability to maintain or enter into new partnerships or strategic collaborations; and the factors described under “Risk Factors” in Zymeworks’ quarterly and annual reports filed with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for its quarter ended September 30, 2023 (a copy of which may be obtained at www.sec.gov and www.sedar.com). Although Zymeworks believes that such forward-looking statements are reasonable, there can be no assurance they will prove to be correct. Investors should not place undue reliance on forward-looking statements. The above assumptions, risks and uncertainties are not exhaustive.

Furthermore, we are in the process of finalizing our financial results for the fourth quarter and fiscal year 2023, and therefore our finalized and audited results and final analysis of those results are not yet available. The preliminary expectations regarding year-end cash, cash equivalents, and marketable securities are the responsibility of management, are subject to management’s review and the actual results could differ from management’s expectations. The actual results are also subject to audit by our independent registered public accounting firm and no assurance is given by our independent registered public accounting firm on such preliminary expectations. You should not draw any conclusions as to any other financial results as of and for the year ended December 31, 2023, based on the foregoing estimates.

Forward-looking statements are made as of the date hereof and, except as may be required by law, Zymeworks undertakes no obligation to update, republish, or revise any forward-looking statements to reflect new information, future events or circumstances, or to reflect the occurrences of unanticipated events.

Zymeworks: A Differentiated Product Pipeline Built on Unique Capabilities in Antibody Engineering and Medicinal Chemistry

Seeking to address unmet patient needs in HER2+ GI Cancers

zanidatamab
(HER2 bispecific antibody)

- Licensed to Jazz and BeiGene
- **BTC 2L**: rolling USA regulatory submission underway with breakthrough designation
- **GEA 1L**: pivotal Phase 3 top-line data readout in H2 2024
- Additional ongoing and planned clinical studies beyond BTC and GEA

5 new INDs planned
Focus on Gyn CA, Lung CA, & GI CA

- **ZW171 (IND 2024)**
  MSLN x CD3 bispecific antibody
- **ZW191 (IND 2024)**
  FRα TOPO1i ADC
- **ZW220 (IND 2025)**
  NaPi2b TOPO1i ADC
- **ZW251 (IND 2025)**
  GPC3 TOPO1i ADC
- **IND5 TBD (IND 2026)**
  Candidate nomination expected in in H2 2024

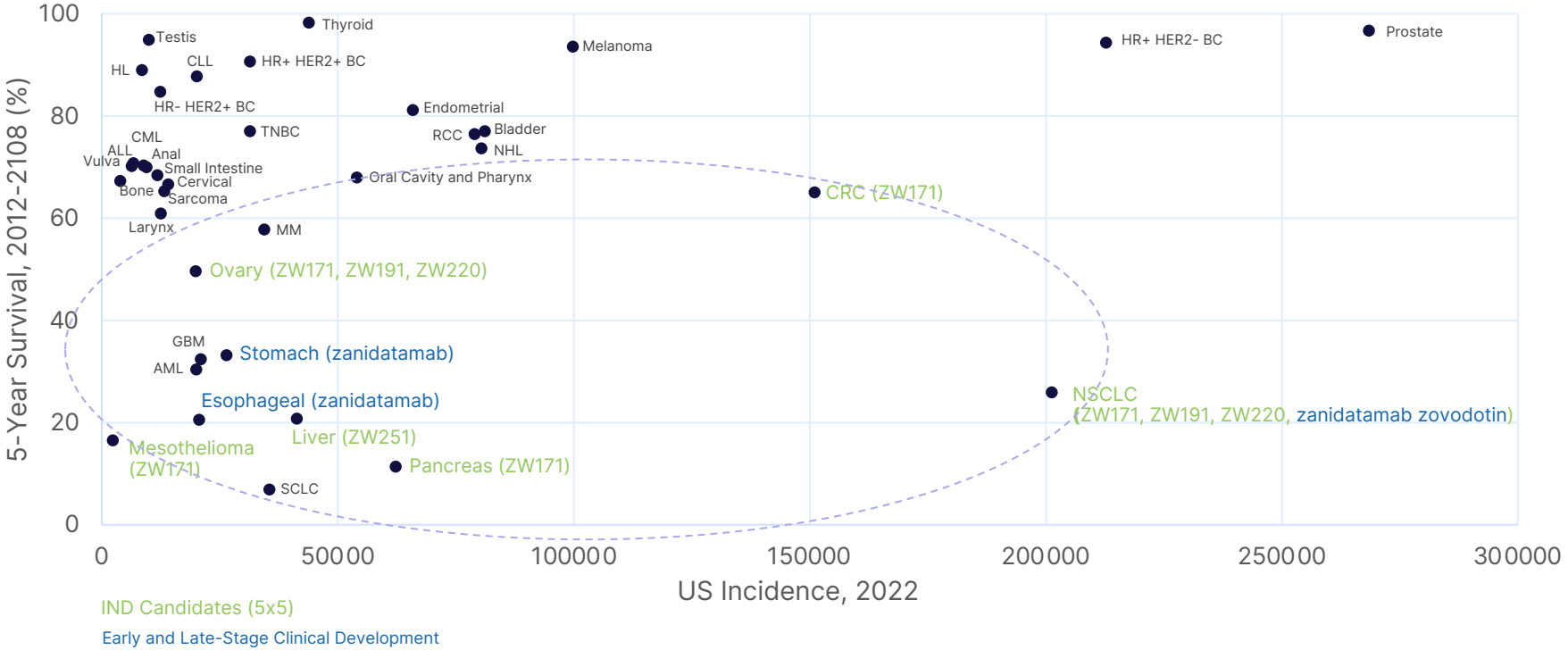
Continuing to innovate and move beyond oncology

- Unique/differentiated platform to build nextgen **ADC**'s and **TriTCE**'s
- Therapeutic focus to be expanded into **autoimmune and inflammatory disease (AIID)**
- Research scope to potentially expand into multifunctional engineered cytokines and dual checkpoint inhibitors

Expanding product pipeline with potential near-term approval and launch of zanidatamab
Cash runway forecast into H2 2027

1L: first-line (treatment); 2L: second-line (treatment); ADC: antibody drug conjugate; BTC: biliary tract cancers; CD3: cluster of differentiation 3 protein complex and T cell co-receptor; FRα: folate receptor alpha; GEA: gastroesophageal adenocarcinoma; GPC3: glypican-3; HER2: human epidermal growth factor receptor 2; IND: investigational new drug (application); MSLN: mesothelin; NaPi2b: sodium-dependent phosphate transporter 2b; NSCLC: non-small cell lung cancer; TOPO1i: topoisomerase 1 inhibitor.

R&D Focus on Cancers With Highest Unmet Medical Need



CRC: colorectal cancer; SEER*Explorer, accessed 10 Oct 2022.

Extensive Potential News Flow over 2024 and 2025

PIPELINE EVENTS

H1 2024

- Expect to complete USA and China regulatory submission for zanidatamab in 2L BTC
- Anticipate commencement of Phase 3 confirmatory study for zanidatamab in 1L BTC
- Phase 2 study for zanidatamab zovodotin in NSCLC (over-expressing HER2)
- Expected IND filing for first 5x5 candidate

H2 2024

- Alignment with FDA on the confirmatory trial in 1L metastatic BTC; Jazz expects it will be open and enrolling patients prior to the completion of the rolling BLA submission
- Expected pivotal Phase 3 top-line data readout in GEA 1L
- China potential regulatory decision for zanidatamab in 2L BTC
- Expected IND filing for second 5x5
- Nomination of 5th product candidate in 5x5

2025

- Potential USA and China launch for zanidatamab in BTC and initial royalty revenue from partners Jazz and BeiGene
- Expected IND filing for ZW220 (NaPi2b)
- Expected IND filing for ZW251 (GPC3)

PUBLICATIONS & CONFERENCES

- ASCO GI (January 18-20)
- JSMO (February 22-24)
- World ADC London (March 12-15)
- AACR (April 5-10)
- PEGS (May 13-17)
- ASCO (May 31-June 4)
- WCGQ (July 3-6)
- ESMO (September 13-17)
- EORTC-NCI-AACR (October 23-25)
- SITC (November 6-10)
- SABCS (December 10-14)

Manuscripts: Overview of ZD06519 (TOPO1i payload) and full clinical data for *A Dose Finding Study of ZW49 in Patients With HER2-Positive Cancers* (NCT03821233)

Illustrative. Key news flow only.

Projected Cash Runway Supports R&D Priorities into H2-2027

Current Financial Status:

- Cash resources of approx. **$455 MM*** (as of December 31, 2023)
- Includes recent private placement of $50 MM to EcoR1 Capital

Potential sources to extend cash runway into H2 2027:

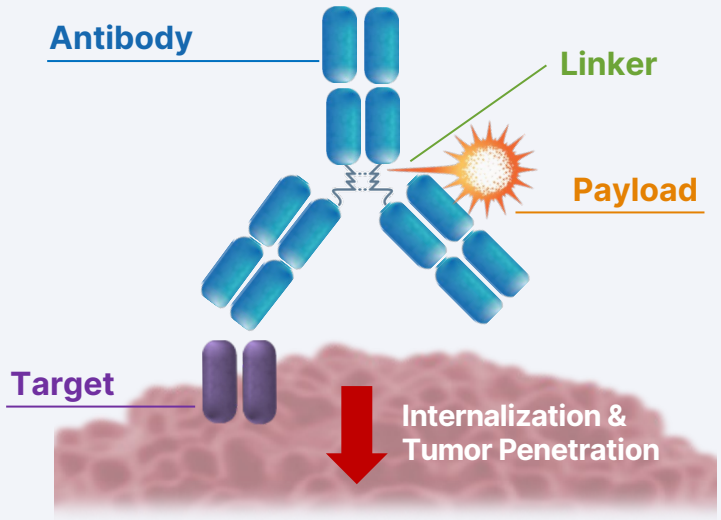
- Additional regulatory approval milestones for zanidatamab
- Royalties and commercial milestones from zanidatamab from Jazz and BeiGene sales
- Additional payments from legacy technology platform collaborations
- New partnerships/collaborations to provide upfront payments and committed R&D funding

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

Antibody-Drug Conjugate (ADC) Program

Building Next-Generation ADCs

Core Competencies Utilized in Next-Generation ADC Design



- 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, such as target-mediated binding and **enhanced internalization**. Biparatopic and bispecific ADC formats may also provide future differentiated therapeutics
- Utilize 3D cancer cell line spheroid models to select optimal ADC antibodies based on **tumor spheroid penetration and cytotoxicity**

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

1. Colombo R, Rich JR. Cancer Cell 2022 (40), 1255-1263 ; 2. Colombo R, Barnscher SD, Rich, JR. Cancer Res 2023, 83 (7). Abstract #1538 presented at AACR 2023.

Differentiated Development of Antibody-Drug Conjugates

Designing next-generation antibody-drug conjugates 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
ZW191	Gynecological cancers, NSCLC, TNBC	FRα	Topoisomerase-1 Inhibitor (ZD06519)	8		On track for IND filing in 2024			
ZW220	OVCA, NSCLC	NaPi2b	Topoisomerase-1 Inhibitor (ZD06519)	4		On track for IND filing in 2025			
ZW251	Hepatocellular carcinoma	GPC3	Topoisomerase-1 Inhibitor (ZD06519)	4-8		On track for IND filing in 2025			
Zanidatamab zovodotin	NSCLC	HER2	Auristatin (ZD02044)	2		NCT03821233	On track for Initiation of Phase 2 in NSCLC in 2024		
XB002 (ICON-2)	Solid tumors	Tissue Factor	Auristatin (ZD02044)	4		NCT04925284			EXELIXIS[1] mid-single digit royalty

1 Agreement with Iconic; XB002 in-licensed by Exelixis.
OVCA: ovarian cancer; TNBC: triple-negative breast cancer.

ZW191
FRα-targeting ADC

FRα is found in ~75% of high-grade serous ovarian carcinomas[1] and ~70% of lung adenocarcinomas[2]

Optimized Design[3]
- IgG1 antibody selected for its enhanced internalization and tumor penetration
- Novel moderate potency topoisomerase-1 inhibitor payload with bystander activity (ZD06519)
- Drug-to-antibody ratio ~ 8
- Validated peptide cleavable linker sequence

Differentiated Profile
- Differentiated anti-tumor activity in preclinical tumor models with a breadth of FRα expression[1]
- Favorable safety profile in non-human primate toxicology studies[3]
- Opportunity to treat broader range of FRα-expressing cancers

Next Milestone
- Expected IND filing in 2024

1. Köbel, M., Madore, J., Ramus, S. et al. Br J Cancer 111, 2297–2307 (2014).
2. O'Shannessy DJ, et al., Oncotarget. 2012 Apr; 3(4):414-25
3. Lawn S et al. Abstract # 2641 Presented at AACR 2023

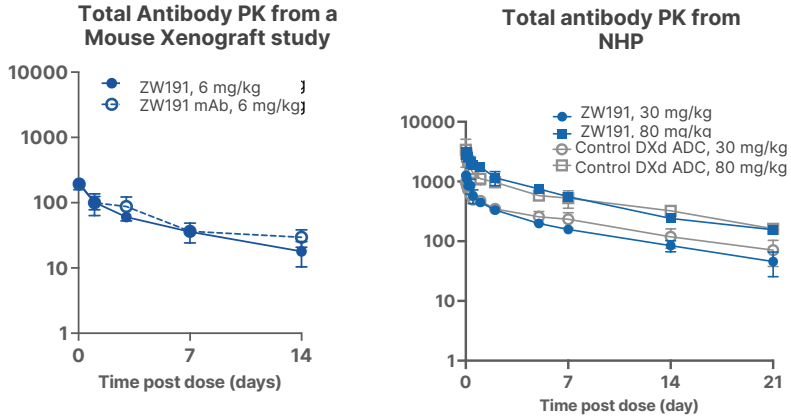
ZW191: Novel and Proprietary TOPO1i Payload Well-Tolerated

ZW191 is well-tolerated in non-human primate (NHP) at 30 mg/kg

Dose mg/kg q3w x2	Tolerated?	Histopathology; Clinical Chemistry; Hematology
30	Yes	Thymus, stomach; AST ↑; ABRETIC↓
80	No	Thymus, kidney, testis, and brain; AST ↑; BUN ↑; ABRETIC↓; ABLYMP↓

- MTD ≥ 30 mg/kg in a 2-dose non-GLP NHP toxicology study
- Histopathology findings at 30 mg/kg were considered as background/low severity and not adverse
- Clinical chemistry and hematology findings at 30 mg/kg considered mild and/or non-dose responsive
- At 30 mg/kg, clinical observations were limited to fecal abnormalities, with no effect on body weight

ZW191 has a favorable pharmacokinetic (PK) profile



- **ZW191 displays favorable PK** and is **well tolerated in NHP at exposure levels** above those projected to be efficacious
- GMP process development is underway to support an expected 2024 IND filing

GMP: good manufacturing practices; MTD: maximum tolerated dose; NHP: non-human primates

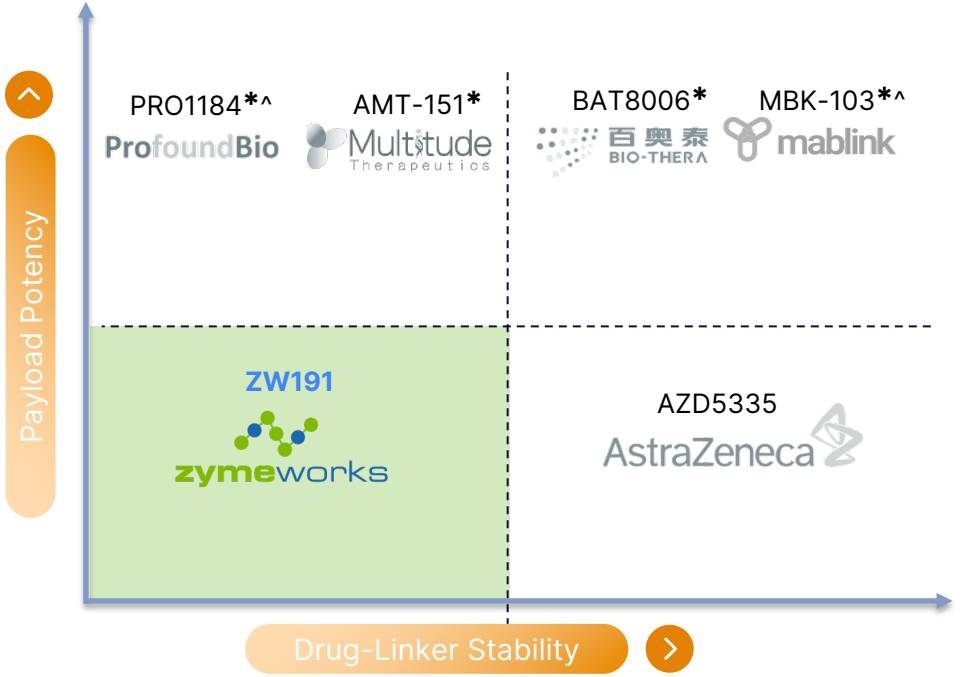
Lawn S et al. ZW191, a novel FRa-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload. Abstract # 2641 presented at American Association for Cancer Research annual meeting 2023.

Differentiation is Critical for ZW191 in the Competitive FRα ADC Space for TOPO1i

The right design to target FRα

1. **Potential best-in-class antibody**
   The ZW191 antibody was selected for enhanced internalization, payload delivery, and tumor penetration.[1]
2. **Topoisomerase-1 inhibitor (TOPO1i) payload mechanism**
   TOPO1i containing ADCs have proven to be an effective mechanism to treat ovarian cancers.[2,3]
3. **Moderate payload potency**
   A moderate potency TOPO1i payload (ZD06519) was selected for ZW191 to enable a higher protein dose, which may be advantageous for target engagement, tumor penetration, and drug exposure.[5] Exatecan is 3-10X more potent than the ZW191 payload.
4. **Moderate antibody-linker stability**
   A 'designed instability' approach was taken with ZW191; all approved ADCs feature an element of linker instability.[4]
5. **Strong bystander activity**
   Strong bystander activity is beneficial when treating tumors with low and heterogenous expression of FRα.[1]

The balance between **drug-linker stability** and **payload potency** differentiates ZW191 from other FRα-TOPO1i ADCs



*** Denotes use of exatecan payload**
^ Denotes use of Fc-silenced antibody

1. Lawn S et al. Abstract # 2641 Presented at AACR 2023; 2. Meric-Bernstam F, et al., Journal of Clinical Oncology 2023 41:17; 3. Moore K, et al., j.annonc.2023.09.1924; 4. Colombo R, Barnscher SD, Rich JR. Cancer Res 2023, 83 (7). Abstract #1538 presented at AACR 2023 5. Lawn S. ZW191: A Potential Best-in-Class TOPO1i ADC for Treatment of FRα-Expressing Solid Tumors, Presented at World ADC London 2023.

ZW220
NaPi2b-targeting ADC

NaPi2b is found in >95% of ovarian serous adenocarcinomas[1] and >85% of non-small cell lung adenocarcinomas[1]

Design[2]
- IgG1 antibody selected for its strong binding and internalization
- Moderate potency topoisomerase-1 inhibitor payload with bystander activity (ZD06519)
- Intermediate drug-to-antibody ratio ~ 4
- Validated peptide cleavable linker sequence

Profile
- Strong preclinical activity in models with a breadth of NaPi2b expression[1]
- Encouraging tolerability in repeat dose non-human primate toxicology studies[2]
- First-in-class ADC potential for NaPi2b-expressing solid tumors

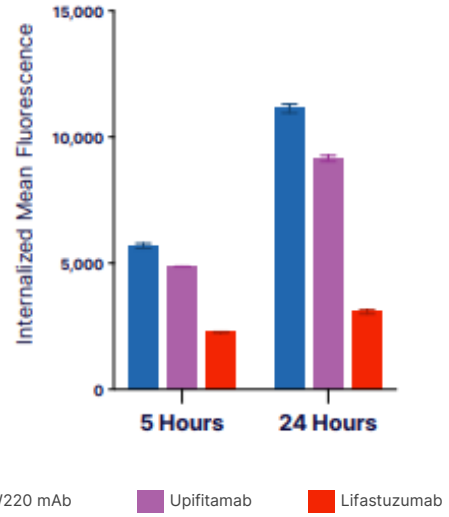
Next Milestone
- Expected IND filing in 2025

1. Lin K, et al. Clin Cancer Res. 2015;21(22):5139–5150
2. Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023

ZW220: Potential Utility in Multiple Cancers; On Track for Clinical Studies in H1-2025[1,2]

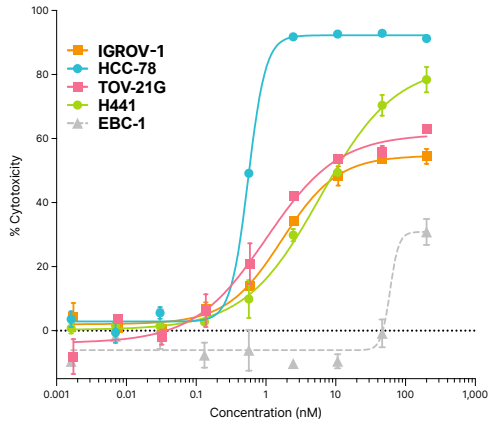
Customized format for function with best-in-class and first-in-class potential

Efficient and Rapid Internalization



Growth Inhibition in Ovarian Cancer and NSCLC Models

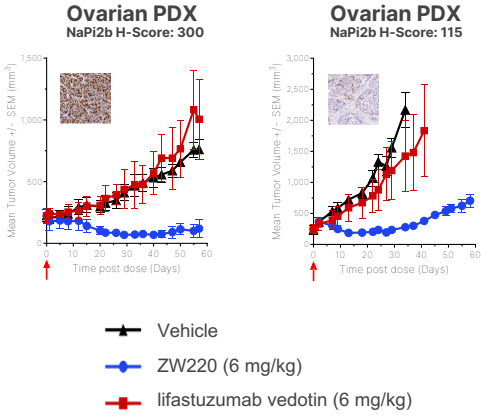
ZW220 DAR 4 cytotoxicity in 3D spheroids



Representative dose-response cytotoxicity curves for ZW220 DAR 4, relative to untreated, in a panel of NaPi2b$^{+/-}$ tumor cell line spheroids.

Anti-Tumor Activity in Ovarian Cancer Models

Anti-tumor activity of ZW220 and lifastuzumab vedotin against ovarian patient derived xenografts (PDXs) expressing high and low NaPi2b



Cell line spheroids with NaPi2b/Cell expressed: IGROV-1 (Ovarian) 1,770,00 expressed; HCC-78 (NSCLC) 820,000 expressed; TOV21G (Ovarian) 350,000 expressed; H441 (NSCLC) 41,000 expressed; EBC-1 (NSCLC) 0 expressed.

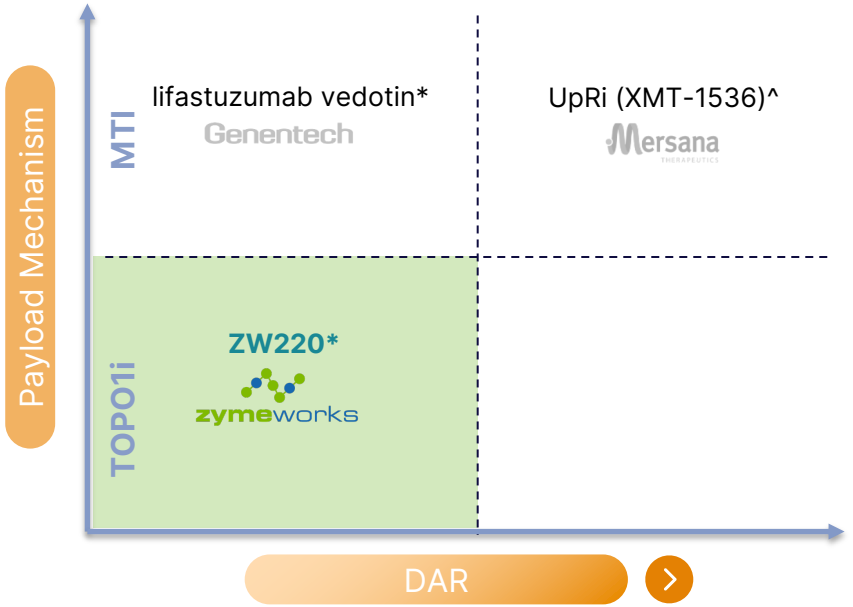
1. Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023; 2. Hernandez Rojas A et al. Presentation at World ADC 2023.

ZW220: Designed to Address Challenges Encountered With Other NaPi2b ADCs

The right design to target NaPi2b

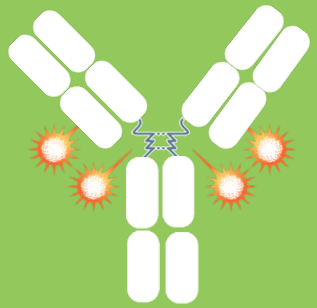
1. **Topoisomerase-1 inhibitor (TOPO1i) payload mechanism**
   TOPO1i containing ADCs have proven to be an effective mechanism to treat ovarian cancers.[1,2]
2. **Intermediate drug-antibody-ratio (DAR)**
   An intermediate DAR (~4) is desirable to enable a high protein dose to maximize target engagement, tumor penetration, and drug exposure.[4] Additionally, an intermediate DAR may help to mitigate on-target off-tumor toxicities.
3. **Strong, persistent bystander activity**
   Strong bystander activity is beneficial when treating tumors with low and heterogenous expression of NaPi2b.
4. **Potential best-in-class antibody with strong internalization**
   The ZW220 antibody was selected for optimal internalization.[3]
5. **Moderate antibody-linker stability**
   A 'designed instability' approach was taken with ZW220; all approved ADCs feature an element of linker instability.[4]

ZW220 combines a **bystander active TOPO1i payload** at a **DAR of 4** with a potential **best-in-class ADC antibody**



* Denotes strong bystander activity of payload
^ Denotes weak or transient bystander activity of the payload

1. Meric-Bernstam F, et al., Journal of Clinical Oncology 2023 41:17; 2. Moore K, et al., j.annonc.2023.09.1924; 3. Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023; 4. Colombo R, Barnscher SD, Rich JR. Cancer Res 2023, 83 (7). Abstract #1538 presented at AACR 2023



ZW251
Glypican 3-targeting ADC

GPC3 is expressed in 76% of hepatocellular carcinomas (HCC)[1]

Design[2]
- An IgG1 antibody with enhanced ADC characteristics
- Topoisomerase-1 inhibitor mechanism of action
- Novel moderate potency payload with bystander activity (ZD06519)
- Intermediate drug-to-antibody ratio ~ 4
- Validated peptide cleavable linker sequence

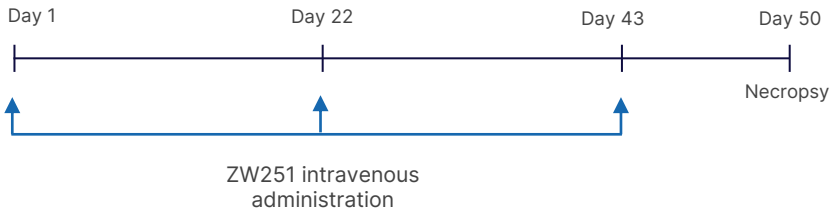
Profile
- Strong preclinical activity in models with a breadth of GPC3 expression[2]
- Noteworthy tolerability in repeat dose non-human primate toxicology studies[2]
- First-in-class ADC potential for HCC
- Glypican 3 is expressed in 76% of hepatocellular carcinomas (HCC), with high expression observed in ~55% of HCC[1]

Next Milestone
- Expected IND in 2025

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

ZW251: Novel and Proprietary TOPO1i Payload Well-Tolerated

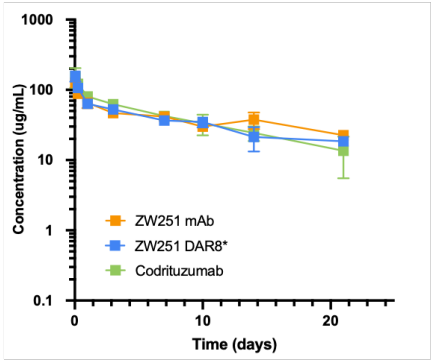
Three Dose Non-Human Primate (NHP) Toxicology Study



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

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

Total IgG in Tg32 Mouse Serum



*Analog utilizes ZW251 mAb conjugated to a closely related linker-payload.

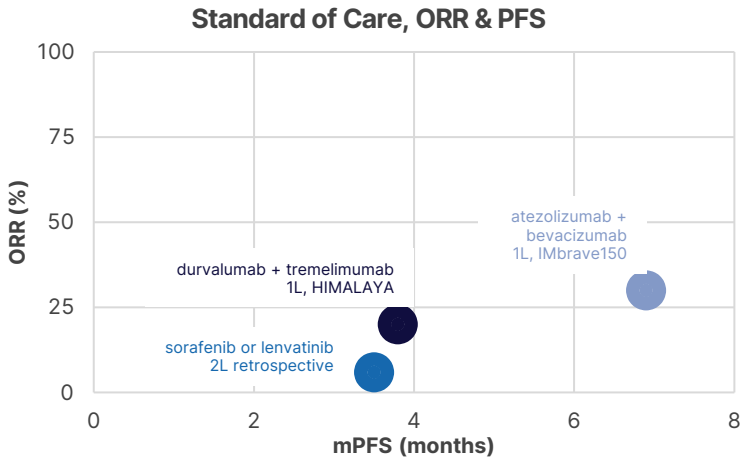
- ZW251 mAb **exhibits comparable PK to a clinical-stage antibody comparator**
- PK of ZW251 mAb **unaffected by conjugation**
- **No mortality was observed** in a repeat dose NHP toxicology study with doses up to 60 mg/kg (DAR 8) or 120 mg/kg (DAR 4)

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

Potential Therapeutic Agent with Alternative Mechanism for HCC Patients

HCC: Limited Treatment Options

- Globally, the sixth most common cancer and third most common cause of death from cancer[1]
- In USA, 1L and 2L SOC provide < 9 months PFS

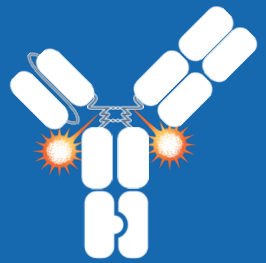


As a potential first-in-class TOPO1i-based ADC for HCC, ZW251 offers the potential of a **new MOA** for patients and an **opportunity to improve upon the current standard of care**

- GPC3 highly expressed in HCC and being targeted by other modalities including TCEs and engineered T-cells.
- ADC approach provides alternate to counter limitations associated with immune-related suppressive HCC microenvironment and a potential therapeutic strategy amenable to combination with SOC.

- ZW251 drug design with potential first-in-class potential
  - Bystander active TOPO1i payload with tailored potency
  - Optimized drug-linker stability and intermediate DAR
  - Strong tumor growth inhibition across tumors displaying range of GPC3 expression

Finn RS et al NEJM 2020; Abou-Alfa GK et al NEJM Evid 2022; Yoo C et al Liver Cancer 2021
1. WHO. International Agency of Cancer Research. Cancer Today. 2020. Available at: https://gco.iarc.fr/today/home. Accessed October 2023 SEER. Cancer Stat Facts. National Cancer Institute. Available at https://seer.cancer.gov/statfacts/



Zanidatamab zovodotin
A Bispecific HER2-targeting ADC

Design
- Novel cross-linking binding designed to enhance internalization of payload and initializes immunogenic cell death (ICD)
- Delivery of novel auristatin payload (ZD02044) covalently linked via a protease cleavable linker in a DAR 2 configuration

Profile
- Differentiated format offers options to overcome potential points of resistance via geometry and cytotoxin; manageable low-grade adverse events; strong inducer of ICD markers and warrants investigation of the combination with checkpoint inhibitors

Next Milestone
- Initiation of Phase 2 in NSCLC

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

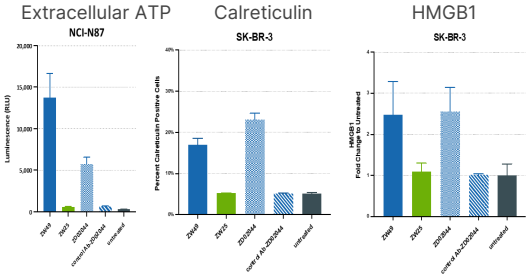
Zanidatamab zovodotin: Summary of Key Potential Differentiators

Pre-clinical data demonstrates potential synergism to combine with immunotherapy. Safety profile from Phase 1 data supports focus in NSCLC population with a recommended dose of 2.5mg/kg Q3W.

Enhanced Internalization of Payload, with ICD

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

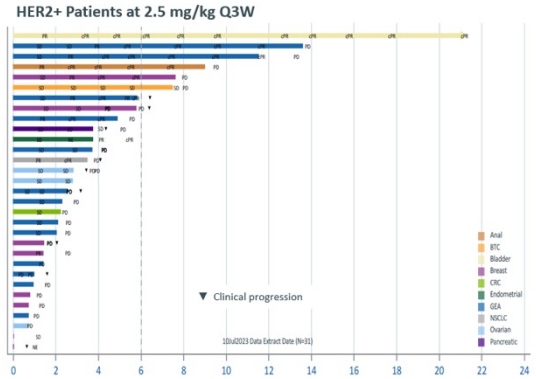
Hallmarks of ICD in HER2 expressing tumor cells



Stronger inducer across hallmarks when compared to trastuzumab based ADCs with DXd or MMAE payloads

Antitumor Activity Across Solid Tumors Including NSCLC

Confirmed ORR of 30%
In 2.5mg/kg Q3W cohort (N=30), median duration of response was 6.8 months with a range of 1.4 – 19.8 months[4]



Differentiated Safety Profile

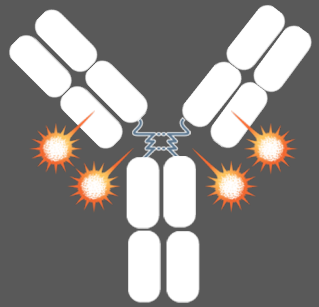
In 67 patients, low grade, manageable adverse events with no ILD or pneumonitis reported[3]

- MTD not reached
- The PK of ADC and total antibody was comparable and appeared to be linear among the three dose regimens examined

Safety: 2.5mg/kg Q3W cohort, N=31[4]

- Gr≥3 TRAEs 16%
- Any grade keratitis of 45%; all cases ↓ to grade 1 or resolved
- Alopecia & IRR: any grade = 16%
- Diarrhea any grade = 29% (No Gr≥3)

Zanidatamab zovodotin is an investigational product that has not received FDA (or any regulatory authority) approval and has not been demonstrated safe or effective for any use.
IHMGB1: high mobility group box 1 protein; ICD: immunogenic cell death; ILD: Interstitial lung disease; IRR: immune related reaction; MMAE: Monomethyl auristatin E; Q3W: every three weeks; TRAE: treatment-related adverse event.
1. Hamblett, KJ et al.,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) 4. Oh Y et al., Abstract# 33234 presented at AACR-NCI-EORTC 2023.



XB002 (ICON-2)
A Novel Tissue Factor Targeting ADC

Design
- Novel antibody that recognizes a Tissue Factor epitope that does not interfere with Factor VII binding
- Delivery of Zymeworks novel auristatin payload (ZD02044) covalently linked via a protease cleavable linker in a DAR 3.8 configuration

Profile
- Differentiated ADC versus Tisotumab Vedotin on tolerability, exposure and combinability

Status
- Phase 1 studies in advanced solid tumors (JEWEL-101)

Multispecific Antibody Therapeutic (MSAT) Program

Driving The Evolution of MSATs

Differentiated Development of Multi-Specific Antibody Therapeutics

Versatile multi-specific antibody therapeutics enhancing 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 and Phase 2 trials (view)				Jazz Pharmaceuticals BeiGene
ZW171 Bispecific T-Cell Engager	Pancreatic, OVCA, CRC	MSLN x CD3 (2+1)	Expected 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

BC: breast cancer; CLDN: claudin; TAA: tumor associated antigen

Zanidatamab: $2B+ Peak Sales Potential*

zymeworks

1 Expect to enter market first in Biliary Tract Cancers (BTC)

- Rolling BLA submission for accelerated approval in 2L BTC
- Expect to complete 1H24, alignment with FDA on confirmatory trial in 1L metastatic BTC

Represents ~12,000 HER2+ cases annually[2] In USA, Europe[3], and Japan

2 Path to approval in 1L Gastroesophageal Adenocarcinoma (GEA) with sBLA

- HER2+/PD-L1 negative: opportunity to address unmet need and replace trastuzumab
- HER2+/PD-L1 positive: opportunity to replace trastuzumab as HER2-targeted therapy of choice
- Opportunity to explore potential in neoadjuvant populations[1]

Represents larger patient opportunity with ~63,000 HER2+ cases annually[2] in USA, Europe[3] , and Japan

3 Expanded opportunity across lines of Breast Cancer (BC)[1]

- Early lines of therapy (neoadjuvant)
- Post T-DXd
- T-DXd ineligible settings
- Novel combinations

Ongoing trials in early breast cancer:

- I-SPY
- MD Anderson collaboration

Considerable market opportunity with more than 150,000 cases annually[4] in USA, Europe[3], and Japan

4 Broad potential beyond BTC, GEA, and BC in multiple HER2-expressing indications

- Colorectal
- NSCLC
- Ovarian
- Endometrial
- Pancreatic
- Bladder
- Salivary Gland
- Ampullary
- And other HER2-expressing solid tumors

*Adapted from Jazz Pharmaceuticals' Guidance

1L = first line, 2L = second line, ASCO = American Society of Clinical Oncology, ASCO GI = ASCO Gastrointestinal Cancers Symposium, BC = breast cancer, BLA = biologics license application, BTC = biliary tract cancer, ESMO = European Society for Medical Oncology, FDA = U.S. Food and Drug Administration, GEA = gastroesophageal adenocarcinoma, HER2 = human epidermal growth factor receptor 2, HCP = healthcare provider, NSCLC = non-small cell lung cancer, PD-L1 = programmed cell death ligand 1, sBLA = supplemental biologics license application, T-DXd = trastuzumab deruxtecan. 1 Pending regulatory approvals, 2 Incidence sources: Kantar reports, ToGA surveillance report; SEER, cancer.gov; ClearView Analysis; GLOBOCAN, Data on file, 3 Major markets, U.K, France, Germany, Spain, Italy, 4 Incidence source estimates derived from multiple sources: Decision Resources Group, Kantar Health, Jazz Market Research, data on file, 5 Funda Meric-Bernstam et al, Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 1, dose-escalation and expansion study, The Lancet Oncology, Volume 23, Issue 12, 2022, Pages 1558-1570, ISSN 1470-2045, https://doi.org/10.1016/S1470-2045(22)00621-0.

Zanidatamab: Summary of Clinical Development Program for BTC and GEA

Clinical Data

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

Single Agent Activity in Second-Line BTC Pivotal Study

- 41.3% ORR (51.6% in the IHC3+ patients), 12.9 months mDoR[1]

Combination Activity in First-Line GEA studies

- 79% ORR with a mDOR of 20.4 months and 84% 18-month OS rate[2]
- 75.8% ORR with mDOR 22.8 months and mPFS 16.7 months[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 clinical data presented at ASCO GI 2023[2] and Phase 1b/2 data at ESMO 2023[3]

Upcoming Milestones

- Planning for potential accelerated approval of zanidatamab in second-line BTC, Jazz has alignment with FDA on confirmatory trial requirements
- Topline data for the Phase 3 HERIZON-GEA-01 trial expected in H2 2024
- Anticipate commencement of Phase 3 confirmatory trial in first-line BTC

Collaboration Partners:

mDOR: median duration of response; ORR: overall response rate; OS: overall survival; mPFS: median progression free survival
1. Harding et al., Lancet Onco 2023; 2. Elimova E et al., Abstract #347 presented at ASCO GI 2023, JCO 41(4S); 3. Lee KW et al., Abstract #3088 presented at ESMO 2023; 4. NCT05152147

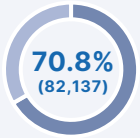
Zanidatamab: Epidemiology of Biliary Tract Cancer

Biliary Tract Cancers (BTC) are molecularly diverse tumors which include gallbladder cancer (GBC), intrahepatic cholangiocarcinoma (ICC), and extrahepatic cholangiocarcinoma (ECC).[1] Gall bladder cancer is the more prevalent diagnoses among BTC cases.[2]

Epidemiology (World)

Incidence varies globally:

- Globally, it was estimated ~210,878 new cases of BTC in 2017, increasing to 219,420 in 2018.[3]
- Occurs at rate between 1-4 cases per 100,000 people / year in most regions; yet some regions exceed this age-standardized annual incidence rate [4,5]
- Chile had the highest incidence, followed by Japan and South Korea (10.83, 8.88, and 8.55/100,000, respectively)[6]



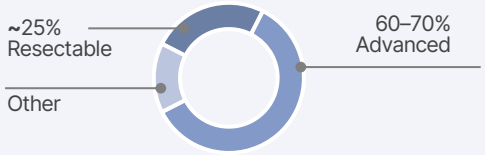
of all estimated new GBC cases occurred in Asia, with 10% (~12,570) in Europe in 2020[7]

Epidemiology (United States)

Most cases are diagnosed at an advanced stage:

- BTC is reported to occur at a rate of 1.2 (GBC), 1.7 (ICC), 1.8 (other) per 100,000 people per year in the United States[8] which is estimated to be ~15,000 patients per year

Cases by stage at diagnosis [9, 10]



Progression

Second-line:

- Survival from first-line treatment is modest, ~35% of patients get second-line, but it ranges by geographical region[11, 12, 13]
- 2L chemotherapy yields response rates of < 10%; mOS of patients is often < 6 months[14] with a recent phase II trial reporting 8.6 months[15]
- ~40-60% of BTC patients have possible targetable alterations with differences between anatomical subgroups[9,16]

19% of GBC
17% of ECC
5% of ICC

} Overexpress HER2[17]

1. Bogenberger JM et al., Precision Oncol. 2018; 2. Lazcano-Ponce EC et al., CA: Cancer J Clin. 2001; 3. Ouyang G et al., Cancer 2021; 4. Tam V et al., Curr. Oncol. 2022; 5. Miranda-Filho A et al., Int. J. Cancer 2020; 6. Zhang Y et al., Cancer Epidemiology. 2021; 7. GLOBOCAN. World fact sheets (GallBladder), 2020; 8. NCI. SEER. SEER*Explorer: Access Feb 2023. conditions included intrahep,Gallb,other; 9. Gómez-España MA, et al., Clin Transl Oncol. 2021; 10. Banales JM et al., Nat Rev Gastroenterol Hepatol. 2020; 11. Rizzo A et al., Anticancer Research, 2019; 12. Chiang N-J et al., Biomolecules. 2021; 13. Fornaro L et al., Br J Cancer. 2014; 14. Lamarca A et al., J Clin Oncol. 2019; 15. Yoo C et al., Final results (NIFTY) abstract 55P presented at ESMO Congress 2022; 16. Bridgewater JA et al., Am Soc Clin Oncol Educ Book. 2016; 17. Galdy S et al., Cancer Metastasis Rev. 2017.

Zanidatamab: Targeted Treatment Options are Rapidly Evolving in BTC

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)[1]

Advanced / Metastatic Biliary Tract Cancers

First-line treatment options[2]

Guideline option from the ABC-02 trial[3]
gemcitabine + cisplatin
ORR = 26%, mPFS = 8.4 months,
mOS = 11.7 months

Guideline option from the TOPAZ-1 trial [4,5]
cisplatin + gemcitabine + durvalumab
ORR = 26.7%$_{IA}$, mPFS = 7.2 months,
mOS = 12.9 months

Recent option from the KN-966 trial[6]
cisplatin + gemcitabine + pembrolizumab
ORR = 29%$_{BICR}$, mPFS = 6.5 months,
mOS = 12.7 months

Progression in Metastatic Biliary Tract Cancers

Second-line treatment options[2]

Guideline option from the ABC-06 trial[7]
FOLFOX ORR= 5%, mPFS= 4.0 months,
mOS = 6.2 months

Is Targeted Treatment More Effective Than Chemotherapy?

FGFR2 fusions+: mPFS= 7.0 – 9.0, mOS= 17.5 – 21.7 months[8]
IDH1 mutation: mPFS = 2.7 months, mOS = 10.3 months[9]

Ongoing Results from HER2 Targeting Agents in 2L+ Trials*

trastuzumab + FOLFOX mPFS = 5.1 months, mOS = 10.7 months[10]
TDXd (HERB trial) mPFS = 5.1 months, mOS = 7.1 months[11]
trastuzumab + pertuzumab (MyPathway) mPFS = 4.0, mOS = 10.9 months[12]

BRAF: activating serine/threonine-protein kinase B-raf kinase; ERBB2: receptor tyrosine-protein kinase erB-2; FGFR2 fusions+: fibroblast growth factor receptor 2 fusions and alterations; FOLFOX: folinic acid, fluorouracil, and oxaliplatin; IDH1: isocitrate dehydrogenase 1; MMR: mismatch repair; MSI: microsatellite instability; NTRK: neurotrophic receptor tyrosine kinase; TDXd: trastuzumab deruxtecan . * have not received FDA (or any regulatory authority) approval for BTC 2L indication.

1.Valle JW et al., Lancet 2021; 2. Vogel A et al., ESMO Open (BTC Guidelines) 2022; 3. Valle JW et al., NEJM 2010; 4. Oh D-Y et al., NEJM Evid 2022; 5. Oh D-Y et al., Annals of Oncol 2022 (33 suppl_7): 6. Kelley K et al., Lancet 2023; 7. Lamarca et al., J Clin Oncol 2019; 8. Vogel A et al., Annu Rev Med 2023; 9. TIBSOVO US PI Aug 2021; 10. Lee, C-K et al., Lancet Gastroenterol. Hepatol. 2023; 11. Ohba A et al., J Clin Oncol 2022 v40, no.16_suppl; 12. Javle M et al., Lancet Oncol 2021.

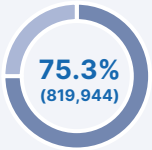
Zanidatamab: Epidemiology of Gastroesophageal Adenocarcinoma

- Gastroesophageal adenocarcinoma (GEA) encompasses gastric (stomach), gastroesophageal junction (GEJ) and esophagus adenocarcinomas
- As of 2020, global incidence rate of gastric cancer is estimated to be 5.6%, while esophageal cancer is 3.1%[1]
- There is a wide geographic variation incidence: 15- to 20-fold difference between high- and low-incidence regions[4]
- Most patients present at a late stage of disease[1,2,3]

Gastric Cancer[1,2]

Globally, ~1.1 million patients diagnosed with an estimated increase of 62% to 1.77 million by 2040

- Majority of gastric cancers are adenocarcinomas (~95%)[5]



of all estimated new gastric cancer cases occurred in Asia in 2020

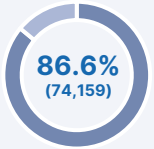
Incidence rates[11]

USA	Europe	Japan
1.2%	3.1%	13.5%

Esophageal Cancer[1,3]

Globally, 604,100 patients diagnosed annually, with an estimated increase by 58.4% to ~957,000 by 2040

- 85,672 esophageal cancer patients were diagnosed with esophageal adenocarcinoma (EAC)



of those patients were diagnosed with EAC in high developed countries in 2020

Incidence rates[11]

USA	Europe	Japan
0.8%	1.2%	2.6%

HER2-Positivity

HER2+ in GEA ranges 7-34%[6,7]

- Men > Women
- Moderate > Poor differentiated
- GEJ (32.2%) > Gastric (21.4%)
- Intestinal > Diffuse subtype

Prognostic significance of HER2 is unclear,[8] and influenced by:

- Intra-tumoral heterogeneity
- Treatment line
- Clonal evolution [8,9,10]

1. Sung H et al., (Globocan 2020) CA Cancer J Clin. 2021; with factsheet https://gco.iarc.fr/today/fact-sheets-populations; 2. Morgan E et al., Lancet 2022; 3. Morgan E et al., Gastroenterology 2022; 4. Sitarz R et al., Cancer Manag Res 2018; 5. Ajani JA, et al., Nat Rev Dis Primers 2017; 6. Gambardella V et al., Ann Oncol 2019; 7. Van Custem E et al., Gastric Cancer, 2015; 8. Ajani JA et al., J Natl Compr Canc Netw 2022; 9. Zhao D et al., J Hematol Oncol 2019; 10. Janjigian YY et al., Cancer discover 2018; 11. incidence rates as a percent of global cancer cases.

Zanidatamab: Targeted Treatment Options For Patients with HER2+ GEA

Summary: First-line treatment guidelines for patients with HER2+ Gastric and GEJ adenocarcinoma[1,2,3,4]

Advanced / Metastatic HER2+ Gastric or GEJ Adenocarcinoma

Guideline option based on the ToGA trial[4]

Doublet chemo (fluoropyrimidine + platinum) ± trastuzumab

ORR = 47 vs 35%
mDOR = 6.9 vs 4.8 months
mPFS = 6.7 vs 5.5 months
mOS = 13.8 vs 11.1 months

NCT01041404

Advanced / Metastatic HER2+ Gastric or GEJ Adenocarcinoma

Guideline option for patients based on Keynote 811 trial[5]
(CPS ≥1 and if no contraindications exist for immunotherapy)

Doublet chemo (fluoropyrimidine & platinum)+trastuzumab ±pembrolizumab

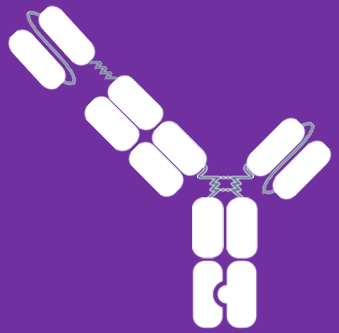
ORR = 73.2 vs 58.4%
mDOR = 11.3 vs 9.5 months
mPFS = 10.9 vs 7.3 months
mOS = 20.5 vs 15.6months

ITT OS was not significant. Early ITT data led to accelerated approval by FDA (ORR: 74vs 52%) May 2021. FDA and EMA approval for PD-L1 CPS ≥1 with *dataset from second and third interim analyses*

NCT03615326

Options for patients with esophageal adenocarcinoma: ToGA (and many other HER2-directed trials in the advanced setting) excluded esophageal adenocarcinoma: in clinic, these patients can be treated with chemotherapy (capecitabine + cisplatin or fluorouracil + cisplatin) + trastuzumab in the first-line setting[1,2]

CPS: combined positive score; GEA: gastroesophageal adenocarcinoma; GEJ: gastroesophageal junction'; HER2+: epidermal growth factor receptor 2 positive; ITT: intention-to-treat population; mDOR: median duration of response; mOS: median overall survival; mPFS: median progression free survival; ORR: median overall response rate; PD-L1: programmed death-ligand 1.
1.Catenacci et al., ESMO Open 2022 7(1) 2.Ajani JA et al., J Natl Compr Canc Netw 2022; 3.Lordick F et al., Ann Oncol 2022; 4.Bang et YJ, Lancet 2010- TOGA updated OS (13.1 vs 11.7months) reported in FDA label, accessed https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/103792s5250lbl.pdf; 5. Janjigian Y et al., Lancet 2023.



ZW171
MSLN x CD3 Multispecific

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

Next Milestone
- Expected IND filing in 2024

scFV: single-chain variable fragment.
1. Afacan N et al., Abstract #2942 presented at AACR 2023.

ZW171: Differentiated Drug Design With Best-In-Class Potential

Mesothelin (MSLN):

- Highly expressed in multiple tumor types including Ovarian, Lung, Pancreatic and Colorectal cancers[1]
- Clinically amenable to T-cell mediated therapy (e.g. Gavo-cel[1]) but limited success with other systemic therapy (e.g. ADCs[2-4], immune toxins[5], prior TCEs[6,7])

Designed to overcome limitations of prior targeted therapies

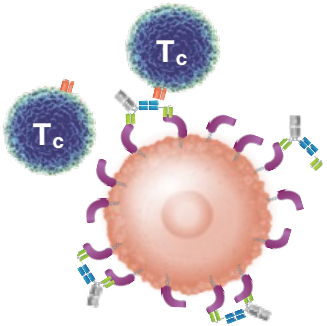
- Avidity dependent MSLN binding enable selective binding and cytotoxicity of high/moderate MSLN expressing cancer cells and spares normal tissue[8]
- Novel CD3 paratope employed to limit cytokine release while supporting effective tumor cell killing[8]
- Format and paratope affinities empirically selected for optimal anti-tumor activity *in vivo*[8]

Anti-MSLN
Bivalent

Anti-CD3
Low affinity

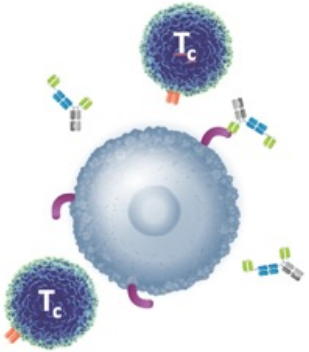
ZW171

Designed to engage cancer cell (MSLN^{high})



ZW171 drives antitumor activity through MSLN and T-cell co-engagement

Designed to avoid healthy cell (MSLN^{low})



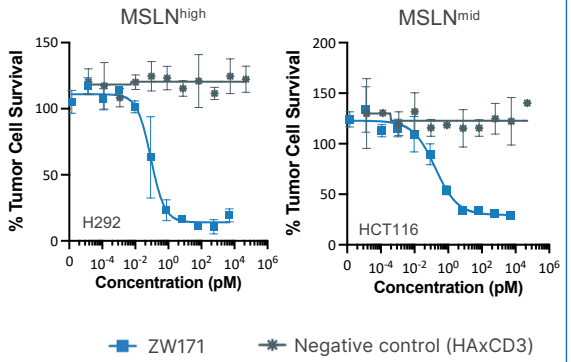
No T-cell activity on normal tissue or periphery as no MSLN engagement

1. Hassan, R., et al. Nat Med 2023, 29, 2099–2109; 2. Kindler et al. Lancet Oncol 2022. 23(4):540-552; 3. Rottey et al. Clin Cancer Res 2022. 28(1):95-105; 4. Weekes et al. Mol Cancer Ther. 2016 15(3):439-447; 5.Hassan et al. Cancer 2020. 126(22):4936-4947; 6. Harpoon Therapeutics Investor Presentation February 2022; 7. Molloy M., et al. Clin Cancer Res. 2021.27(5):1452–1462 8. Piscitelli S. Engineering and Preclinical Development of ZW171: A 2+1 Format Anti-MSLN T Cell Engager, presented at PEGS Boston Summit 2023.

ZW171: Key Design Considerations; On Track for Clinical Studies in 2024

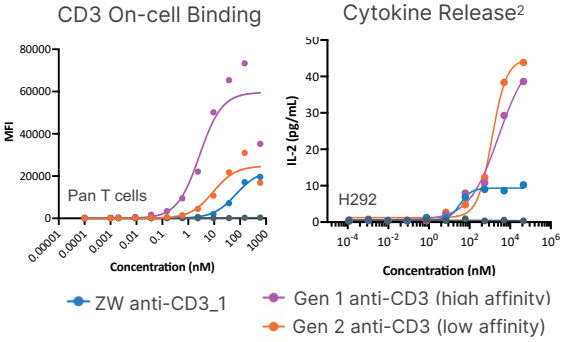
Engineered with 2+1 Format
Facilitates Avidity-Driven Binding[1]

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



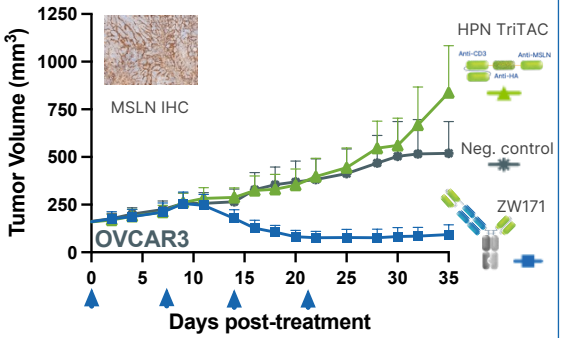
Novel CD3 Paratope with Enhanced Safety

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)

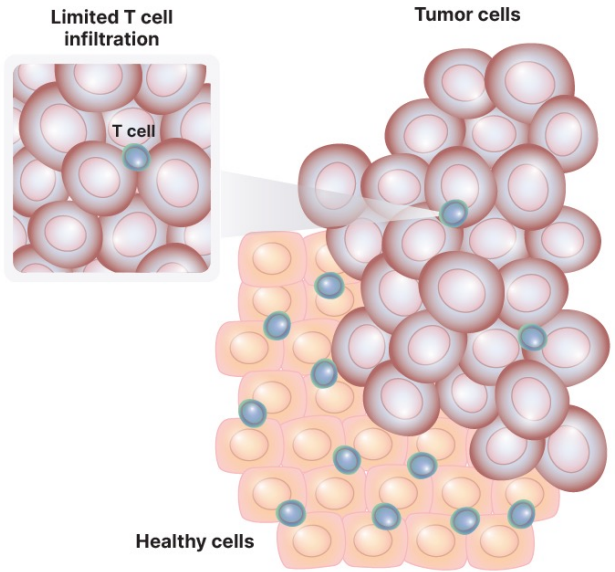
bsAb: bispecific antibody; gen: generation.
1. Afacan N et al., Abstract #2942 presented at AACR 2023; 2. Cytokine release from T cell dependent cytotoxicity assay with pan T cells and H292 tumor cells at 5:1 E:T.

Multispecific Antibody Therapeutic Development

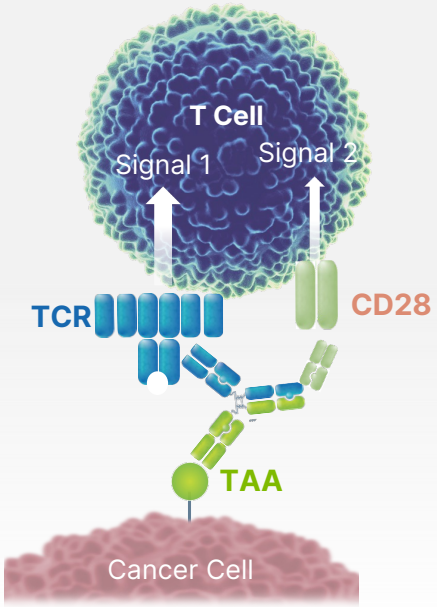
TriTCE Co-Stimulatory Therapeutic Program

Zymeworks Trispecific Co-Stimulatory TCE: Overcoming Lack of Efficacy and Durability of Responses in Solid Tumors by Optimization of Signal 1 and 2

Low T cell infiltration and T cell anergy remain challenges in the treatment of solid tumors



Zymeworks Trispecific Co-stimulatory Program



Provides Signal 1 (CD3) and Signal 2 (CD28) in one molecule **to increase T cell activation and proliferation**

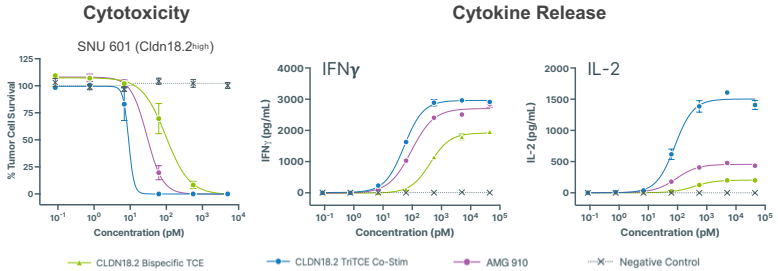
Engineered to balance signal 1 and 2 for optimized **TAA-dependent T cell activation** and expansion

TriTCE Co-stim have the potential **to provide more durable responses** and reinvigorate T cell responses in 'cold' tumors with lower T cell infiltration

Arvedson T et al Ann Rev Cancer Biol 2022

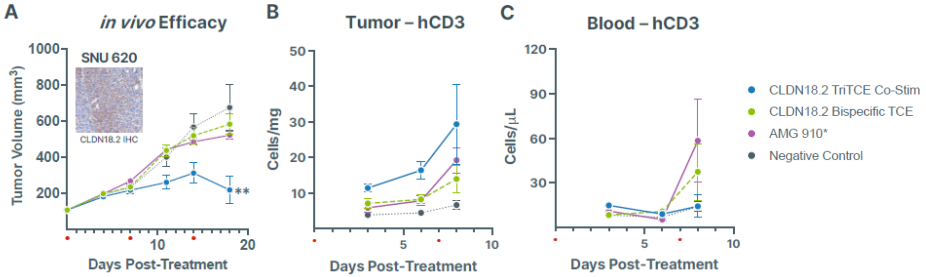
TriTCE Co-Stim Mediates Enhanced *in vitro* and *in vivo* Antitumor Activity Compared to Bispecific TCE and Clinical Benchmark

TriTCE Co-Stim mediates enhanced *in vitro* cytotoxicity and CD28-mediated cytokine activity

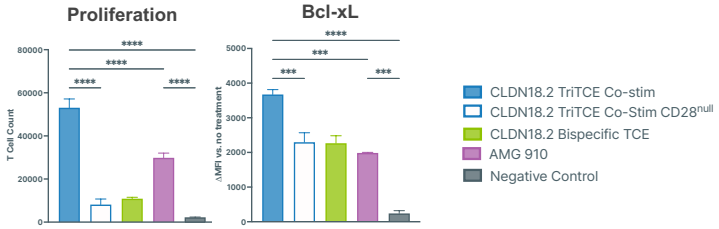


*No cytokine release observed with T-cells alone

TriTCE Co-Stim mediates superior *in vivo* antitumor activity and enhanced intertumoral T cell expansion compared to bispecific clinical benchmark

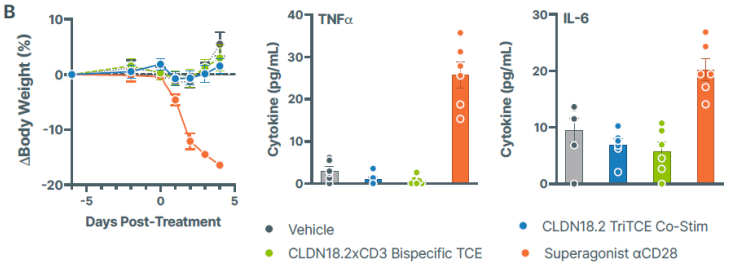


TriTCE Co-Stim enhances T-cell proliferation and survival



TriTCE Co-stim may provide more durable responses in solid tumors

TriTCE Co-Stim is well tolerated in a humanized mouse model of CRS



Newhook L., et al. 2023. AACR. Orlando, FL; Newhook L., et al. 2023. SITC. San Diego, CA

TriTCE Co-Stim: Differentiated Co-Stimulatory (CD28) Platform vs. Clinical Competitors

Co-stimulatory (CD28) TCE Strategies	Zymeworks' Advantage and Limitations of Alternative Strategies
Zymeworks TriTCE Co-stim [1,2]	✓ Zymeworks TriTCE Co-Stim provides **balanced CD3 and CD28 activation** to prevent overactivation of T cells [1,2] ✓ **No CD28 binding in absence of CD3 engagement**, potentially low risks of CD28-mediated immune related adverse events (irAEs) and **demonstrated safety** in in vitro and in vivo CRS models [1,2] ✓ Platform optimized for **TAA-dependent activity** including **low T cell binding and no T cell activation in periphery** [1,2]
CD28xTAA Bispecific (e.g. Regeneron, Xencor)	❑ Optimized for strong CD28 agonism, potentially difficult to optimize by dose adjustment [3,4] ❑ Dependent on presence of signal 1 primed T-cells in TME [3,4] ❑ Potential for severe irAEs in combination with anti-PD-1, similar to CPI toxicities [5,6,7,8,9]
CD3xTAA + CD28xTAA Bispecific Combinations (e.g. Regeneron, Janssen, Roche)	❑ Increased development and challenging dose optimization requirements for two molecules [10] ❑ Potential for CD28 bispecific irAEs [6] ❑ Challenging TAA pairs or non-overlapping epitope targets requirements [3]
CD28xCD3xTAA Trispecific (Sanofi)	❑ High affinity CD3 and CD28 paratopes, activation of peripheral T cells [11,12] ❑ T cell binding and TMDD observed in the periphery [11,12] ❑ CD28 paratope based on CD28 super-agonist, potentially limiting application [11,12]

[1] Newhook et al., Cancer Res. (2023); [2] Newhook et al., JITC (2023); [3] Skokos et al., Sci. Transl. Med. (2020); [4] Dragovich et al., Cancer Research (2023); [5] Stein et al., Journal Clinical Oncology (2023); [6] Martins et al., Nature Reviews Clin Oncol (2019); [7] Eastwood et al., BJP (2010); [8] Roemer et al., Blood (2011); [9] Hui et al., Science (2017); [10] Humphrey et al. (2011) J Natl Cancer Inst.[11] Seung et al., Nature (2022); [12] Promsote et al., Nature Communications (2023)

ADVANCE Portfolio Framework

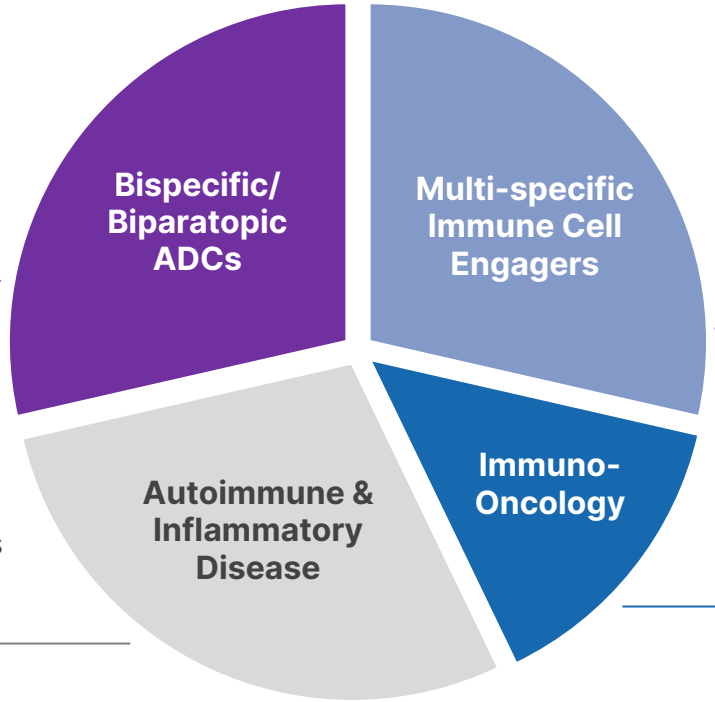
Advancing design of ADCs and Multi-specifics to address complex disease states
Continue to apply technology to hard-to-treat cancers and expand utility to additional therapeutic applications

ADCs

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

AIID

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



Multi-specific Cell Engagers

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

Additional IO

- Cytokine Engineering
- Multifunctional Immune Modulators

Potential for 2 IND-Ready Molecules Per Year From 2027+

Differentiated, Multifunctional Antibody Therapeutics for Oncology and Other Potential Diseases with the Greatest Unmet Patient Need

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

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

Potential to expand beyond oncology to AIID patients

Integrated R&D Engine

5x5 portfolio provides diversity and multiple opportunities for success with 5 new IND's expected by 2026

ADVANCE provides opportunity for further innovation and broader R&D scope with 2 potential IND's annually from 2027+

Desired Product Profile

First and second-line market opportunities

Pursuing products with global peak sales potential >$1 BN

Strategy to retain US commercial rights and collaborate in ex-US markets

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

Company Contacts

Investor Relations

Shrinal Inamdar
Director, Investor Relations
ir@zymeworks.com
+1 604 678 1388

Media Relations

Diana Papove
Senior Director, Corporate Communications
media@zymeworks.com
+1 604 678 1388