Making a Meaningful Difference

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

Investor and Analyst Presentation

MAY 2024

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This presentation and the accompanying 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' expectations regarding implementation of its strategic priorities; the anticipated benefits of its collaboration agreements with Jazz, BeiGene and other partners, 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; the timing and status of ongoing and future studies and the related data; anticipated preclinical and clinical data presentations; expectations regarding future regulatory filings and approvals and the timing thereof; the timing of and results of interactions with regulators; potential safety profile and 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; Zymeworks' ability to satisfy potential regulatory and commercial milestones with existing and future partners; the timing and status of ongoing and future studies and the release of data; anticipated continued receipt of revenue from existing and future partners; Zymeworks' preclinical pipeline; anticipated sufficiency of existing cash resources and certain anticipated regulatory milestone payments to fund Zymeworks' planned operations into the second half of 2027; expectations for future investigational new drug and foreign equivalent applications submissions 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 (copies of which may be obtained at www.sec.gov and www.sedarplus.ca).

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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**: Our partner Jazz completed rolling USA regulatory submission seeking accelerated approval
- **GEA 1L**: Jazz is targeting pivotal Phase 3 top-line data readout in late 2024
- 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
- **Candidate 5 TBD (IND 2026)**
  Pre-clinical TriTCE candidate nomination expected in 2H 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

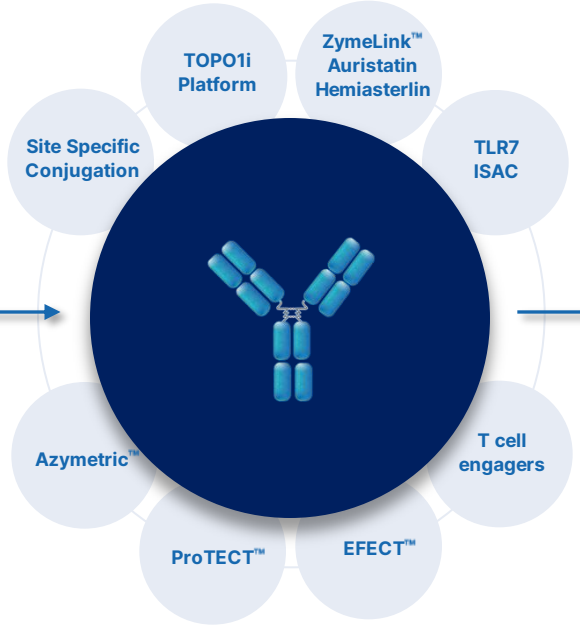
Expanding product pipeline with potential near-term approval and launch of zanidatamab.
Cash runway forecast into 2H 2027, with receipt of certain anticipated regulatory milestone payments.

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

Unique Capabilities in Protein Engineering Provide Opportunity for Differentiated Pipeline of ADCs and Multispecific Antibodies

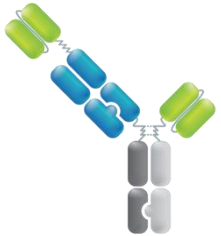
Select Difficult-to-Treat Cancers and Target

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 a single molecule
- Synergistic biology
- Precision targeting through multivalency

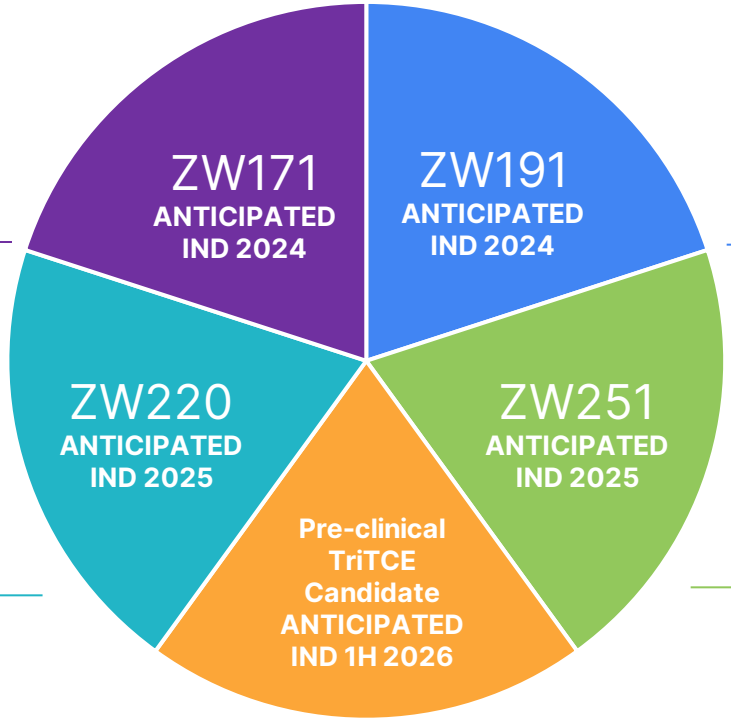
5 **New** INDs expected by 2026

DAR: drug to antibody ratio; ISAC: immune stimulating antibody conjugate; MOA: mechanism of action; TLR7: toll-like receptor 7.

5x5 R&D Strategy: Diversified Portfolio Beyond Zanidatamab with Multiple Opportunities for Success

ZW171 (MSLN)
Bispecific T Cell Engager (2+1) targeting ovarian, NSCLC, and other mesothelin-expressing cancers

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

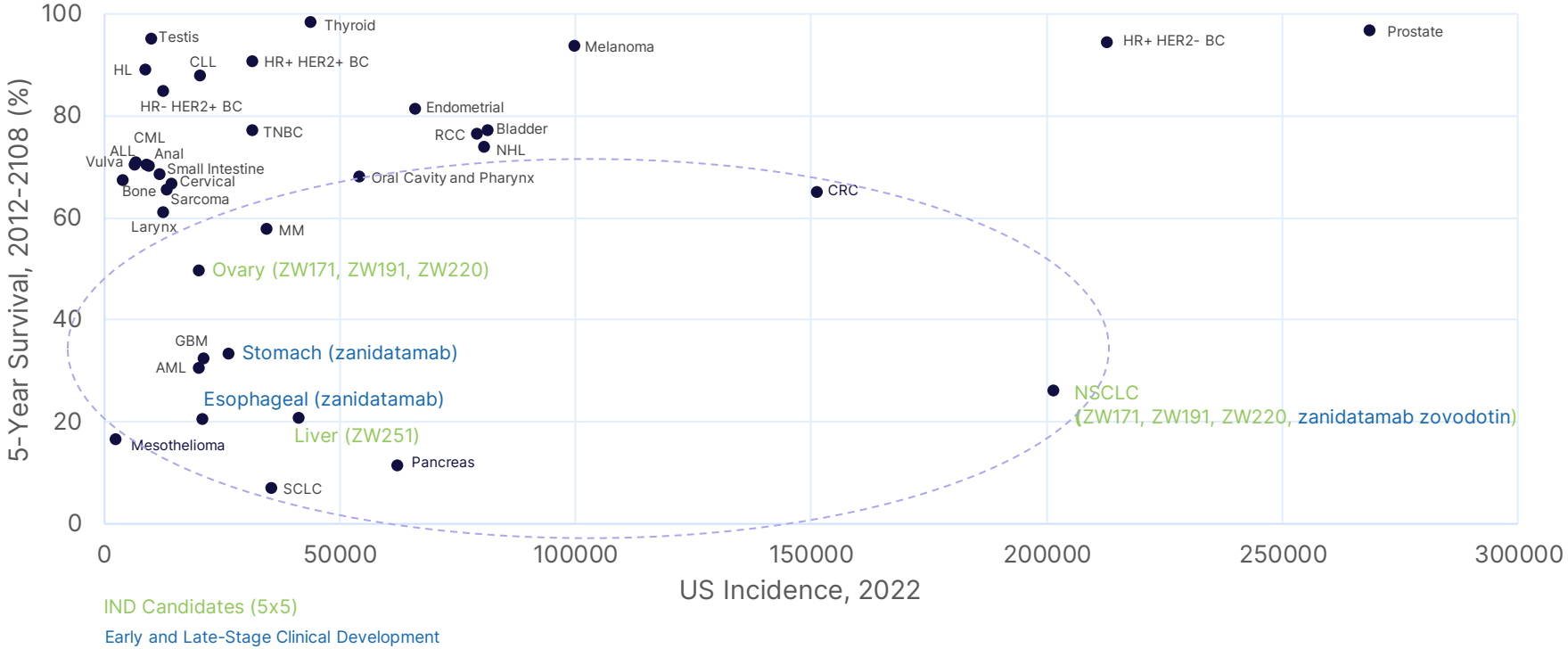


ZW191 (FRα)
Antibody-Drug Conjugate targeting folate receptor alpha expressing tumors including ovarian, other gynecological, and non-small cell lung cancer

ZW251 (GPC3)
Antibody-Drug Conjugate targeting GPC3-expressing hepatocellular carcinoma

TriTCE: trispecific t cell engager.

R&D Focus on Cancers With Highest Unmet Medical Need



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

Extensive Expected News Flow over 2024 and 2025

1H 2024

PIPELINE EVENTS

- Our partner Jazz completed the US regulatory submission for zanidatamab seeking accelerated approval in 2L BTC
- Jazz initiated a Phase 3 global confirmatory trial for zanidatamab in 1L BTC
- Jazz guided that their plans to submit an MAA to the EMA for zanidatamab in BTC are proceeding
- Expected IND submission for first 5x5 candidate

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)

Manuscripts: Overview of ZD06519 (TOPO1i payload)

2H 2024

PIPELINE EVENTS

- Pivotal Phase 3 top-line data readout in GEA 1L targeted by our partner Jazz in late 2024
- Expected BLA submission in China by our partner BeiGene for zanidatamab in 2L BTC
- Jazz expects to initiate a Phase 3 trial for zanidatamab in 2H24 in patients who have progressed on previous T-DXd treatment
- Expected IND submission for second 5x5
- Nomination of 5th product candidate in 5x5

PUBLICATIONS & CONFERENCES

- WCGQ (July 3-6)
- ESMO (September 13-17)
- EORTC-NCI-AACR (October 23-25)
- SITC (November 6-10)
- SABCS (December 10-14)

2025

PIPELINE EVENTS

- Potential USA and China launch for zanidatamab in 2L BTC and initial royalty revenue from partners Jazz and BeiGene
- Expected IND submission for ZW220 (NaPi2b)
- Expected IND submission for ZW251 (GPC3)

Illustrative. Key news flow only.
AACR: American Association for Cancer Research; ASCO: American Society of Clinical Oncology; ASCO GI: ASCO Gastrointestinal Cancers Symposium; BLA: biologics license application; EORTC-NCI-AACR: EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics; EMA: European Medicines Agency; ESMO: European Society for Medical Oncology; JSMO: Japanese Society of Medical Oncology; MAA: marketing authorization application; PEGS: Protein Engineering Summit; SABCS: San Antonio Breast Cancer Symposium; SITC: Society for Immunotherapy of Cancer; T-Dxd: trastuzumab deruxtecan; World ADC: World Antibody Drug Conjugates Summit; WCGI: World Congress on Gastrointestinal Cancer.

Projected Cash Runway Supports R&D Priorities into 2H 2027

Current Financial Status:

- Cash resources[1] of approx. $420.5M (as of March 31, 2024)
- Anticipated cash runway into 2H 2027, which includes certain anticipated regulatory milestone payments

Potential sources to extend cash runway into 2H 2027:

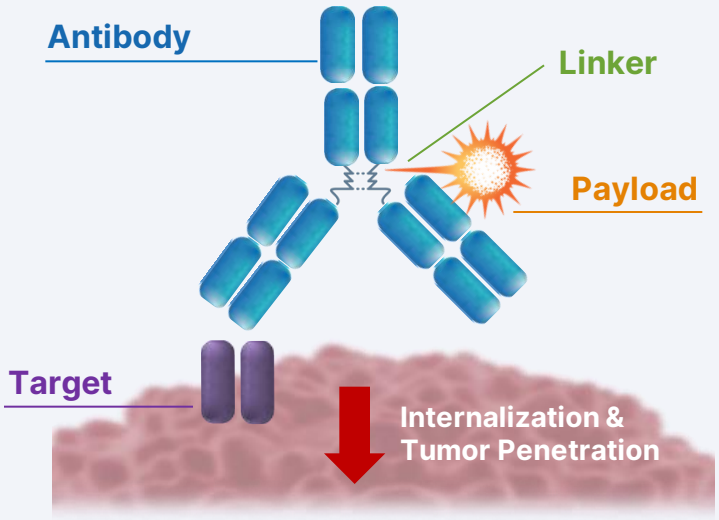
- Additional regulatory approval and commercial milestones for zanidatamab from Jazz and BeiGene
- Tiered royalties between 10-20% from Jazz and 10-19.5% from BeiGene sales (up to 20% when royalty reduction of 0.5% reaches cap in the low double-digit millions of dollars)
- Additional payments from legacy technology platform collaborations
- Potential new partnerships/collaborations to provide upfront payments and committed R&D funding

1. Cash resources consist of cash, cash equivalents, and marketable securities.

Antibody-Drug Conjugate (ADC) Program

Building Next-Generation ADCs

Core Competencies Utilized in Next-Generation ADC Design

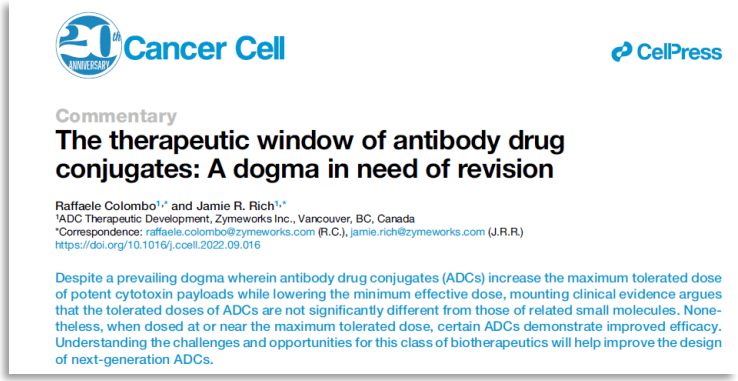


- Focusing on **validated targets** provides opportunity for benchmarking in preclinical development and expected clinical differentiation; novelty of targets anticipated to increase over time
- Exploiting our **proprietary TOPO1i payload (ZD06519)** while exploring alternate mechanisms of action for 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 I 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.

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

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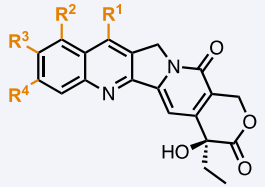
https://doi.org/10.1016/j.ccell.2022.09.016

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

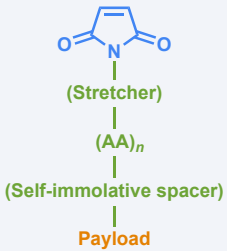
- Acknowledges complex mechanisms driving TOPO1i ADC action
- Sufficient tolerability to achieve ADC dose > 5 mg/kg



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

Colombo R, Rich JR. Cancer Cell 2022 (40).

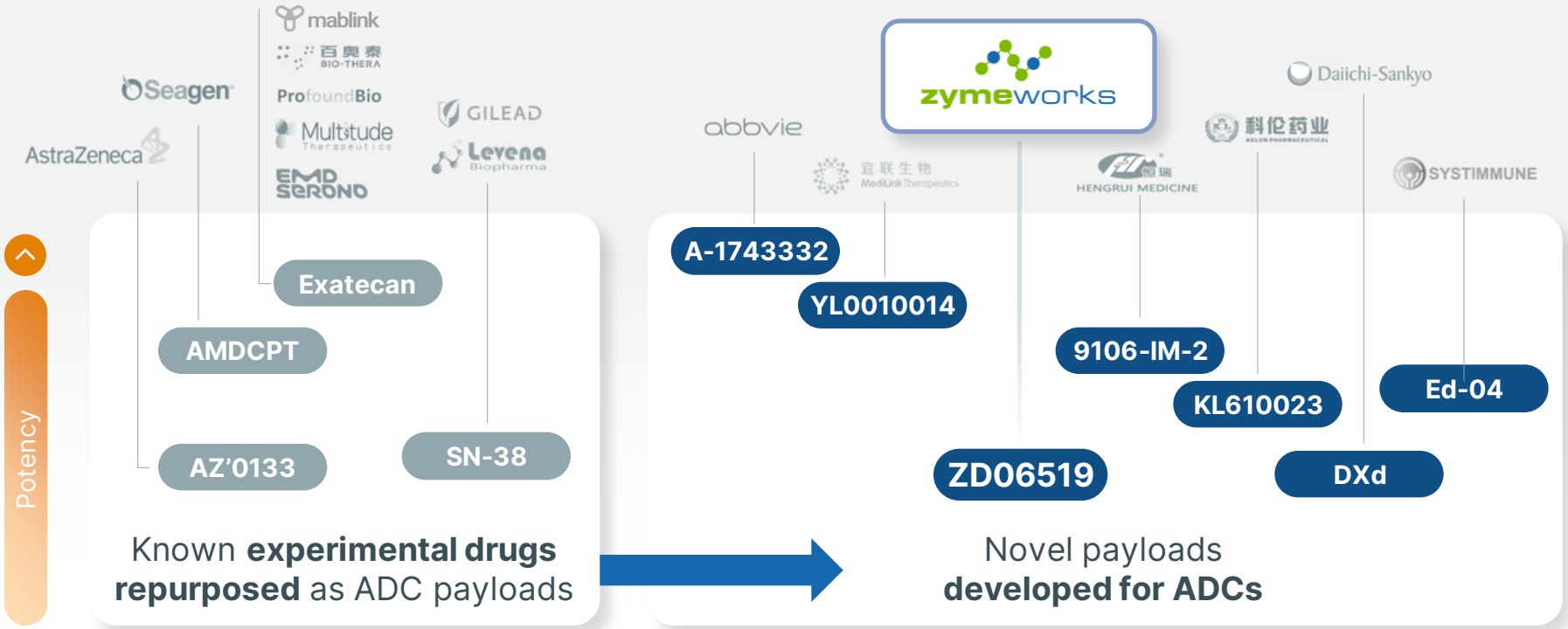
Differentiated Development of Antibody-Drug Conjugates

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	OVCA, other gynecological cancers, NSCLC	FRα	Topoisomerase I Inhibitor (ZD06519)	8		On track for IND filing in 2024			
ZW220	OVCA, NSCLC	NaPi2b	Topoisomerase I Inhibitor (ZD06519)	4		On track for IND filing in 2025			
ZW251	Hepatocellular carcinoma	GPC3	Topoisomerase I Inhibitor (ZD06519)	4		On track for IND filing in 2025			
Zanidatamab zovodotin	NSCLC	HER2	Auristatin (ZD02044)	2		NCT03821233			
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.

Zymeworks Novel Camptothecin Payload Was Selected With ADCs In Mind



Design of novel payloads enables incorporation of properties tailored for ADC mechanism

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 I 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

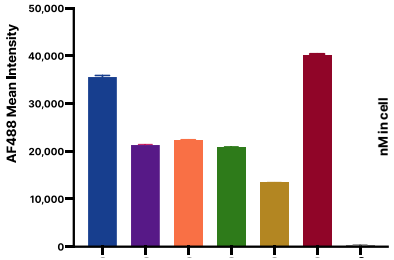
- Expected IND filing in 2024

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.

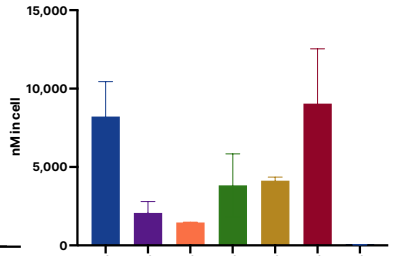
ZW191: Key Design Considerations; On Track for Clinical Studies in 2024

ZW191's novel mAb Drives Superior Internalization, Payload Delivery, and Tissue Penetration

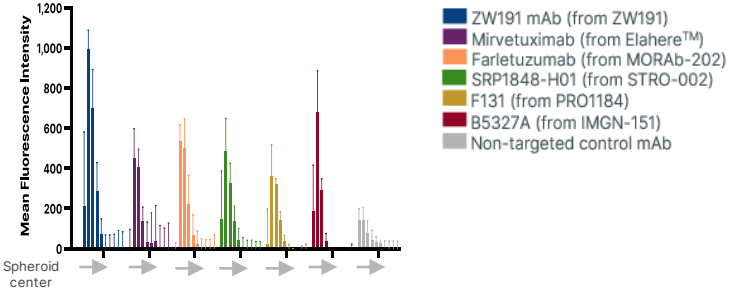
Internalization



Payload Delivery



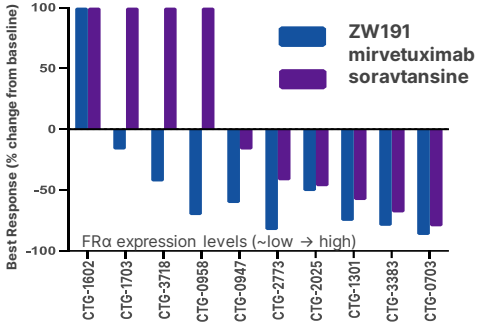
Tumor Spheroid Penetration

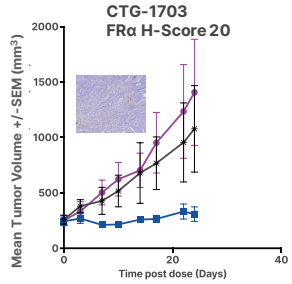


In vitro functional assessment of the antibody properties of ZW191 and other FRα-targeted ADCs and a non-targeted control mAb (all WT Fc to facilitate comparison). Internalization of AF488 labelled antibodies to KB-Hela cells after 24 hrs at 100 nM; Mass-spec. quantification of internalized payload following 24-hour treatment of IGROV-1 cells with 10 nM of ADCs comprising ZW191 mAb or other FRα-targeted mAbs conjugated to ZymeLink® Auristatin (ZLA); Penetration of AF488 labelled antibodies as quantified by high content imaging of spheroid layers at 24 hours post-treatment at 50 nM.

Antitumor Activity Across Multiple Tumor Types And Range of FRα Expression (PDX models)

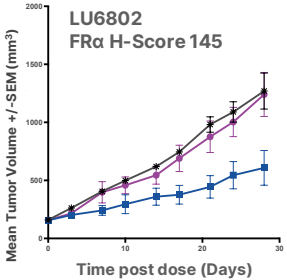
Ovarian Cancer



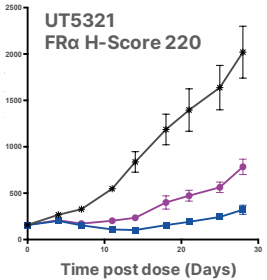


In vivo efficacy of ZW191 and mirvetuximab soravtansine was assessed in Nude or NOD/SCID mice, n=3 per group, single dose 6mg/kg.

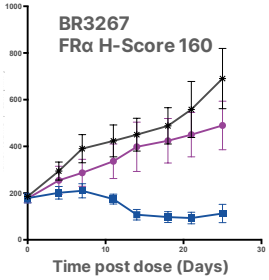
NSCLC



Endometrial



TNBC



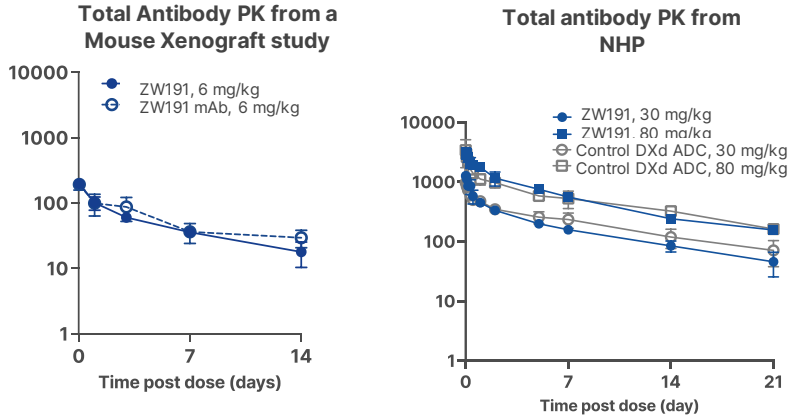
Fc: fragment crystallizable region of antibody; PDX: patient derived xenografts; TNBC: triple-negative breast cancer; WT: wildtype.
Wong J et al., Abstract #3127 presented at American Association for Cancer Research annual meeting 2024; Lawn S. et al. Abstract # 1862 presented at American Association for Cancer Research annual meeting 2024.

ZW191: Novel and Proprietary TOPO1i Payload Well-Tolerated

ZW191 shows a compelling tolerability profile of 60 mg/kg in NHP[1]

Dose mg/kg	Clinical observations	Histopathology	Clinical Chemistry	Hematology & coagulation	Adverse effects	HNSTD
10	None	None	↑ AST, ALT (n=1)	No effects	None	60 mg/kg
30	Emesis/vomitus	↓ Thymic lymphocytes, ↓ PACS	↑ AST, ALT			
60	Liquid/discolored feces Emesis/vomitus ↓ activity level (n=1)	↓ Thymic lymphocytes, ↓ PACS	↑ AST, ALT ↑ CK			

ZW191 has a favorable pharmacokinetic (PK) profile[2]



- No mortality or body weight effects
- No ophthalmic effects
- All effects were non-adverse and reversible
- HNSTD in NHP of 60 mg/kg presents a compelling profile, enabling expectation of achieving efficacious dose level

- **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

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; GMP: good manufacturing practices; HNSTD: highest non-severely toxic dose; MTD: maximum tolerated dose; NHP: non-human primates; PACS: pancreatic acinar cell secretion.

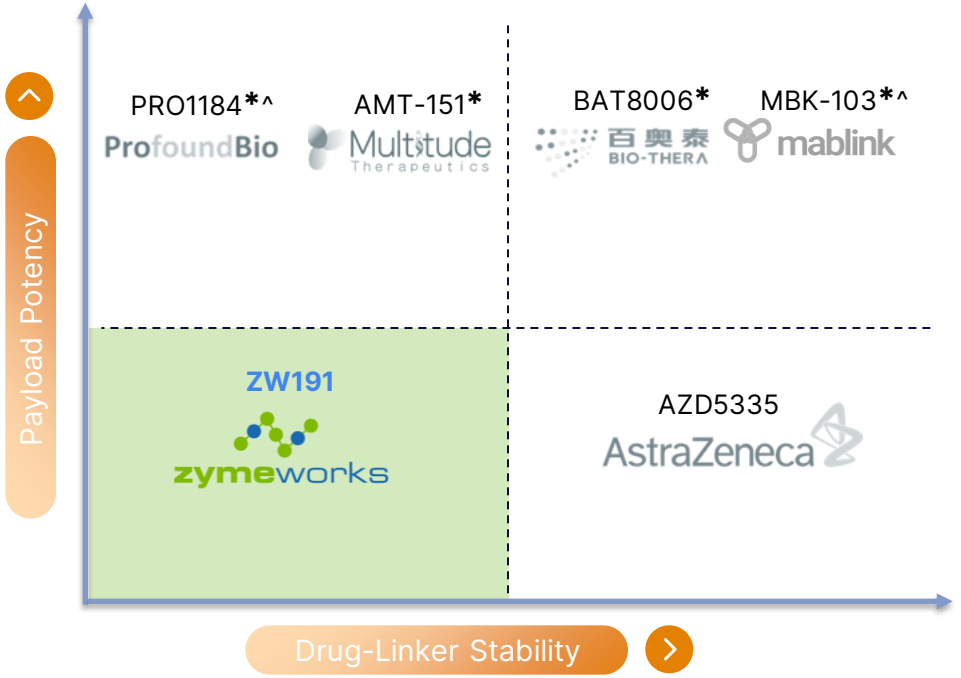
1. Lawn S. et al. ZW191 – a FRα-targeting antibody-drug conjugate with strong preclinical activity across multiple FRα-expressing indications. Abstract # 1862 presented at American Association for Cancer Research annual meeting 2024.
2. Lawn S et al. ZW191, a novel FRa-targeting antibody drug conjugate bearing a topoisomerase-I 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

A novel 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 I 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



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.

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

ZW220
NaPi2b-targeting ADC

NaPi2b is found in ~96% of ovarian serous adenocarcinomas[1] and ~87% of non-small cell lung adenocarcinomas[1]

Design[2]

- IgG1 antibody selected for its strong binding and internalization
- Moderate potency topoisomerase I 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

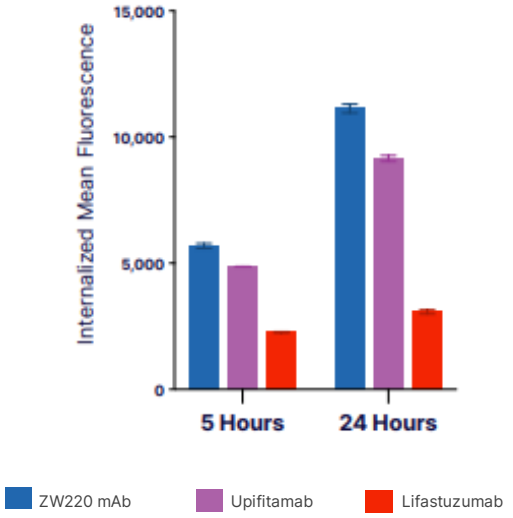
- Expected IND filing in 2025

1. Lin K, et al. Clin Cancer Res. 2015;21(22):5139–5150 (prevalence % based on 26 cases of ovarian serous adenocarcinomas and 31 cases of non-small cell lung adenocarcinomas).
2. Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023.

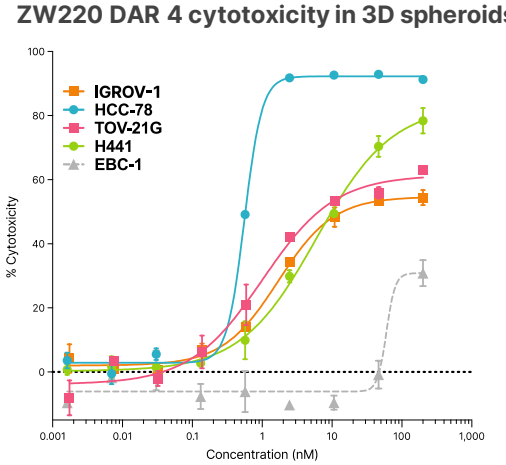
ZW220: Potential Utility in Multiple Cancers; On Track for Clinical Studies in 1H 2025[1,2]

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

Efficient and Rapid Internalization



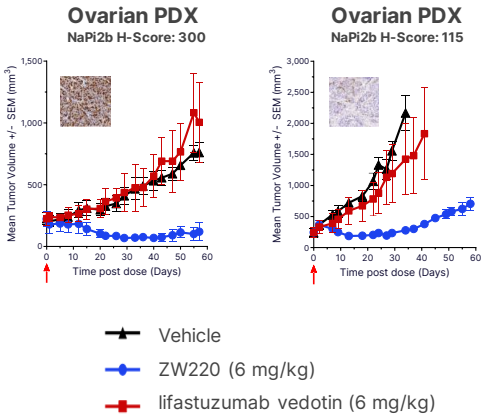
Growth Inhibition in Ovarian Cancer and NSCLC Models



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.
Data generated with ZW220 wildtype (wt) fragment crystallizable region of antibody (Fc).

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

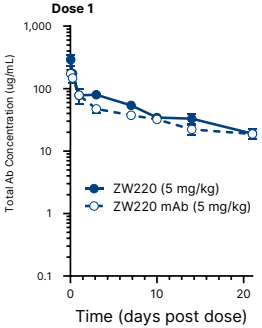
ZW220: Novel and Proprietary TOPO1i Payload Well-Tolerated

ZW220 3-dose non-GLP NHP toxicology study, Q3Wx3				
Test article	**Dose**	**Tolerated?**	**Histopathology; Clinical Chemistry; Hematology**	**MTD**
ZW220	30 mg/kg	Yes	None	90 mg/kg
	60 mg/kg	Yes	None	
	90 mg/kg	Yes	None	

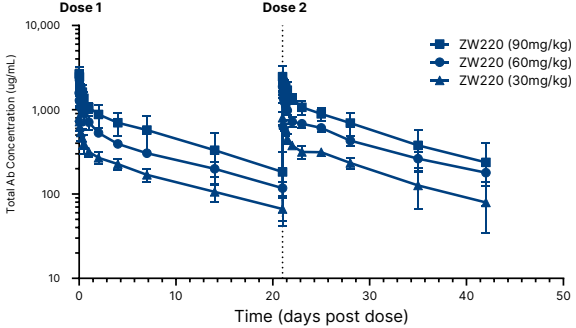
- The MTD of ZW220 in NHPs is 90 mg/kg
- No mortality or adverse pathology findings were observed at high doses

ZW220 has a favorable pharmacokinetic (PK) profile

Total Antibody PK from a Tg32 Humanized FcRn Mice



Total antibody PK from NHP

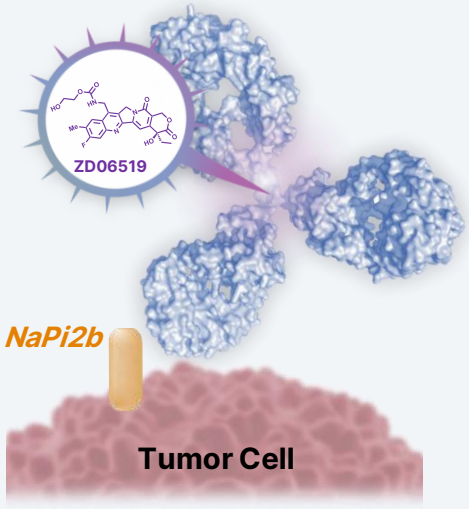


Data generated with ZW220 wildtype (wt) fragment crystallizable region of antibody (Fc).
Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023.

- **ZW220** displays desirable PK characteristics and is well tolerated at high doses
- IND enabling activities are underway

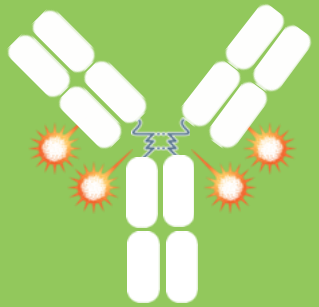
ZW220: A NaPi2b-Targeting Antibody-Drug Conjugate (ADC)

Design



	Design Feature	Benefit
1	**Strong internalizing antibody**	Strong internalization and payload delivery may result in the potential for improved antitumor activity and the ability to target lower levels of NaPi2b
2	**Topoisomerase I inhibitor (TOPO1i) payload mechanism**	Proven ADC mechanism in solid tumors across multiple tumor-associated antigens
3	**Moderate payload potency**	NHP MTD ≥90 mg/kg; potential for high doses in humans
4	**Moderate antibody-linker stability**	Limits antibody-driven toxicities
5	**Strong bystander activity**	Beneficial when treating tumors with low and heterogenous expression of NaPi2b
6	**DAR4**	Balance desired antitumor activity with potential for on-target toxicities
7	**FcγR silenced**	Potential to minimize toxicities driven by cellular uptake via FcγR

FcγR: Fc gamma receptor; FIH: first in human.



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 I 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

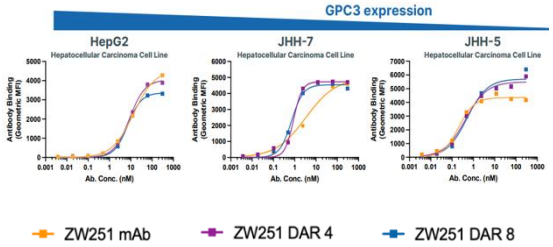
HCC: hepatocellular carcinoma.
1. Wang HL et al., Arch Pathol Lab Med 2008 2.Madera L et al., Abstract #2658 presented at AACR 2023.

ZW251: Potential Utility in Hepatocellular Carcinoma[1,2]; On Track for Clinical Studies in 2025

ZW251 demonstrates target-mediated uptake and anti-tumor activity

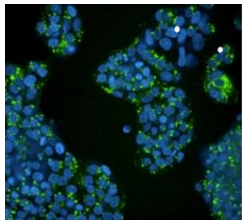
Selected For Strong Binding Over Various Levels Of Expression

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



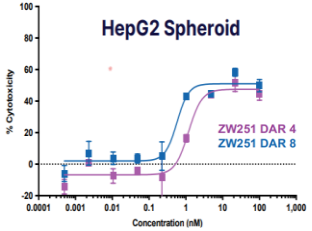
Enhanced ADC Internalization and Cytotoxicity

ZW251 internalized in HepG2 cell line



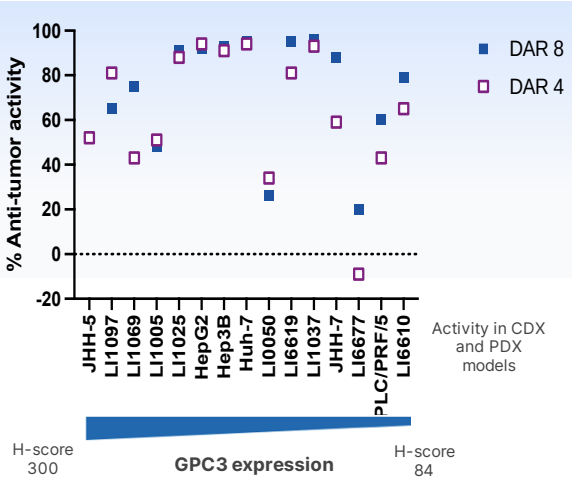
Internalization visualized after 24-hour treatment

Tumor spheroid cytotoxicity in HCC cell line



Cytotoxicity assessed by cell line spheroids (treatment over 4 days)

Differentiated Modality Demonstrates Anti-tumor Activity Across A Range of HCC Models



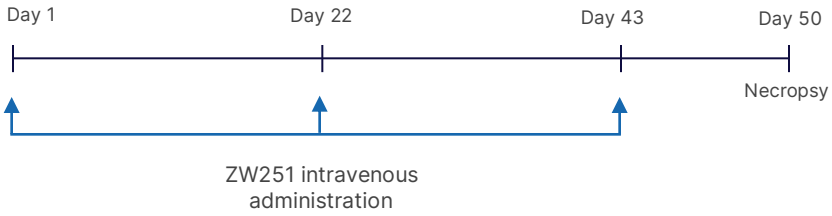
% anti-tumor activity was determined by % tumor growth inhibition (%TGI) calculated as [(1-TVtreatment/TVvehicle) x 100] at Day 21, or at the closest evaluable time point.

CDX: cell derived xenograft.

1. Madera L et al., Abstract #2658 presented at AACR 2023; 2. Madera L et al, presentation at World ADC 2023.

ZW251: Novel and Proprietary TOPO1i Payload Well-Tolerated

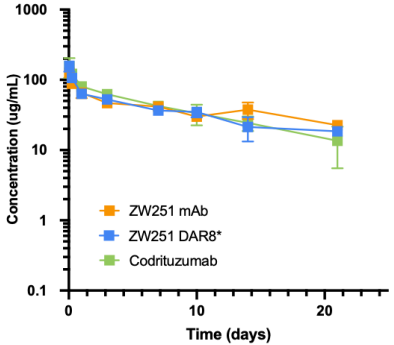
Three Dose Non-Human Primate (NHP) Toxicology Study



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.

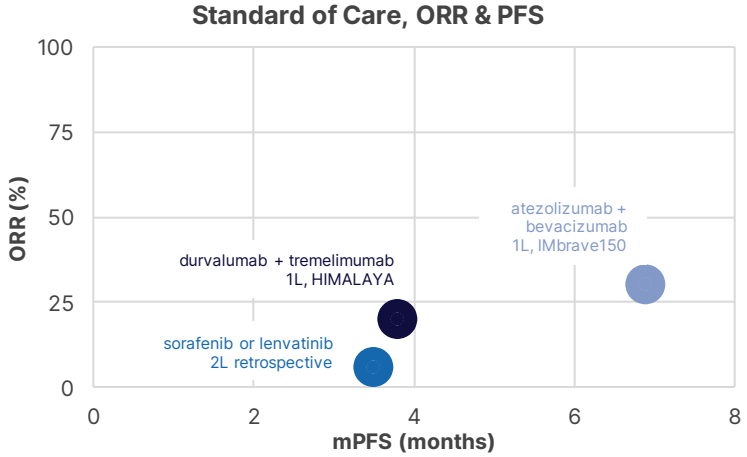
- ZW251 mAb **exhibits comparable PK to a clinical-stage antibody comparator**
- PK of ZW251 mAb **unaffected by conjugation**
- **No mortality was observed** in a repeat dose NHP toxicology study with doses up to 60 mg/kg (DAR 8) or 120 mg/kg (DAR 4)

mAb: monoclonal antibody; PK: pharmacokinetics.
Madera L et al., ZW251, a novel glypican-3-targeting antibody-drug conjugate bearing a topoisomerase I 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, liver cancer is 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

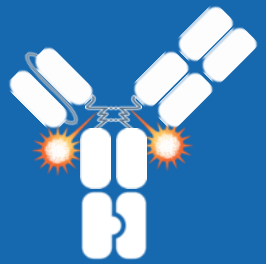


As a potential first-in-class TOPO1i-based ADC for HCC, ZW251 offers the potential of a **new MOA** for patients and an **opportunity to improve upon the current standard of care**

- 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

ORR: objective response rate; PFS: progression-free survival; SOC: standard of care; TCE: T cell engager.
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[1]

- 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; inducer of ICD markers and potential adaptive immune responses, which warrants investigation of its combination with checkpoint inhibitors[2,3]

Next Milestone

- Zanidatamab zovodotin remains ready for a Phase 2 study; however, the initiation of the planned Phase 2 study has been deprioritized

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).

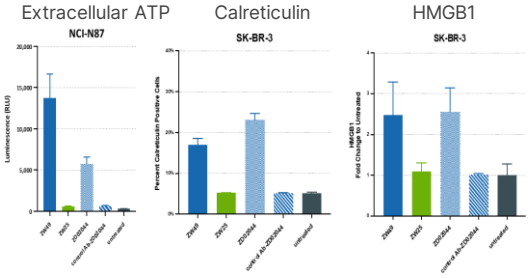
Zanidatamab zovodotin: Summary of Key Potential Differentiators

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]

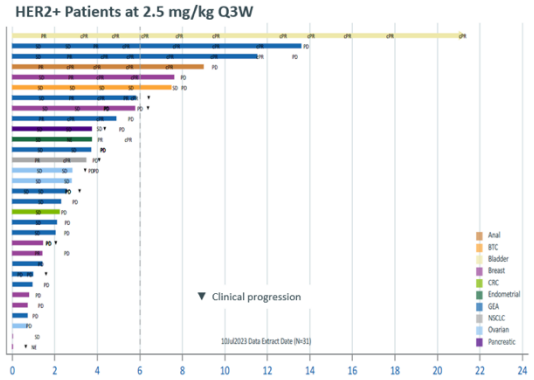
Hallmarks of ICD in HER2 expressing tumor cells



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 Multispecific Antibody Therapeutics

Versatile multispecific 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-302	Jazz Pharmaceuticals, BeiGene
	GEA	HER2 x HER2	HERIZON-GEA-01	Jazz Pharmaceuticals, BeiGene
	BC	HER2 x HER2	EMPOWHER[1]	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	OVCA, NSCLC and other MSLN-expressing cancers	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 DLL3 x CD3 x CD28	IND candidate nomination 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

CD28: cluster of differentiation 28; CLDN: claudin; DLL3: delta-like ligand 3; KLK2: kallikrein-related peptidase 2; PD-L1: programmed cell death ligand 1; TAA: tumor associated antigen.
1. Trial initiation expected in the second half of 2024.

Zanidatamab: $2B+ Peak Sales Potential*

zymeworks

1 Expect to enter market first in BTC (pending regulatory approval)[1]

- Completed rolling BLA submission seeking accelerated approval in 2L BTC
- Confirmatory Phase 3 trial initiated in 1L metastatic BTC

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

2 Path to approval in 1L 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[1]
- 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
- Novel combinations[1]

Ongoing trials in early breast cancer:

- I-SPY2 Trial[4]
- MD Anderson collaboration

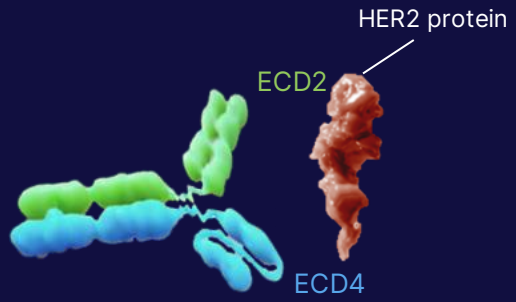
Considerable market opportunity with more than 150,000 cases annually[5] in USA, Europe[3], and Japan

4 Broad potential beyond BTC, GEA, and BC in multiple HER2-expressing indications[6]

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

*Adapted from Jazz Pharmaceuticals' Guidance

sBLA: supplemental biologics license application. 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. NCT01042379; 5. Incidence source estimates derived from multiple sources: Decision Resources Group, Kantar Health, Jazz Market Research, data on file; 6. 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.



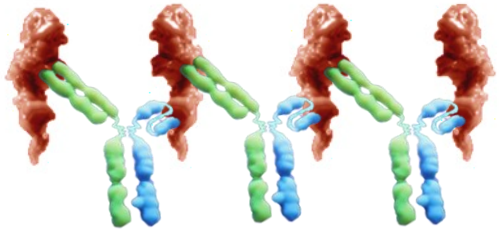
Zanidatamab

A Bispecific Antibody for HER2-Expressing Cancers

Zanidatamab's Unique Format

- Ability to target two distinct HER2 epitopes which 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]
- FDA Breakthrough Designation

Biparatopic HER2-Binding of Zanidatamab Drives Multiple Mechanisms of Action



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

ADCC: antibody-dependent cellular cytotoxicity; ADCP: antibody-dependent cellular phagocytosis; CDC: complement-dependent cytotoxicity; ECD: extracellular domain; FDA: U.S. Food and Drug Administration.

1. Weisser N et al., Nature Communications 2023.

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]

Key Milestones

- Our partner Jazz completed the US regulatory submission for zanidatamab seeking accelerated approval in 2L BTC
- Jazz initiated a Phase 3 global confirmatory trial for zanidatamab in 1L BTC
- Pivotal Phase 3 top-line data readout in GEA 1L targeted by our partner Jazz in late 2024

Collaboration Partners:

mDOR: median duration of response; 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: Licensing Agreement with Jazz

Licensing Agreement Terms[1]	
Counterparty	Jazz Pharmaceuticals
Upfront Payments	$375M received in 4Q22
Regulatory Milestones	Up to $525M
Commercial Milestones	Up to $862.5M
Royalties	**Tiered royalties of 10 to 20% of net sales**
Territories	USA, EU, Japan and all other territories except those in APAC covered by BeiGene agreement
Future R&D Spend	Jazz to fund 100% of costs of future zanidatamab studies

Key Benefits to Zanidatamab Licensing Agreement

- **Meaningful improvement to financial position and reduction in future expenditures** allows focus on growth of exciting early-stage pipeline while zanidatamab advances to commercialization
- **Accelerate** and **expand R&D programs (5x5 and ADVANCE)** while maintaining anticipated cash runway into 2H 2027 with a goal of advancing **5 new programs into clinical studies by 2026**
- **Continued development** of zanidatamab program managed by Jazz
- **Substantial potential milestone payments** based on global regulatory milestones for zanidatamab in BTC and GEA with further upside from royalties and commercial milestones
- **Leverage** Jazz's global commercial infrastructure together with BeiGene's complementary strengths in APAC regions to **optimize commercialization of zanidatamab without requirement for investment in commercial infrastructure** within Zymeworks

APAC: Asia Pacific.
1. All dollar values in US Dollars.

Zanidatamab: Licensing Agreement with BeiGene for Asia Pacific

Licensing Agreement Terms[1]	
Counterparty	BeiGene
Upfront Payments	$40M
Development and Commercial Milestones	Up to $195M
Royalties	**Tiered royalties of up to 19.5% of net sales in BeiGene territories** (up to 20% when royalty reduction of 0.5% reaches cap in the low double-digit millions of dollars)
Territories	Asia-Pacific region (excluding Japan and India)*
Co-development Funding	Currently for BTC and GEA global development

Additional Details

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

1. All dollar values in US Dollars.
* Zymeworks BC granted BeiGene a royalty-bearing exclusive license for the research, development and commercialization of zanidatamab zovodotin in Asia (excluding Japan but including the People's Republic of China, South Korea and other countries), Australia and New Zealand (collectively, the "Territory").

Zanidatamab: Details on Pivotal Studies in BTC and GEA

HERIZON-BTC-01

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

Population: PATIENTS WITH HER2-AMPLIFIED BTC WHO RECEIVED PRIOR GEMCITABINE
N = 100
Cohort 1: 75 with IHC 2+ or 3+
Cohort 2: 25 with IHC 0 or 1+

Regimen: 28 Day Cycles
Day 1: Zanidatamab, 20 mg/kg IV
Day 15: Zanidatamab, 20 mg/kg IV
Imaging every 8 Weeks

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

Primary End Points: ORR (RECIST 1.1 by ICR[1])

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

Additional Details: Meaningful clinical benefit demonstrated including ORR of 41.3%, median DOR of 12.9 months with a mPFS of 5.5 months presented at ASCO 2023, concurrent publication in The Lancet Oncology[2].

HERIZON-GEA-01

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

Population: PATIENTS WITH HER2-POSITIVE ADVANCED OR METASTATIC GEA
N = 918

Regimen: 21 Day Cycles
ARM 1: Trastuzumab + SOC chemotherapy[3], N=238
ARM 2: Zanidatamab + SOC chemotherapy, N=238
ARM 3: Zanidatamab + tislelizumab + SOC chemotherapy, N=238
Imaging every 6 weeks for first 54 weeks, every 9 weeks thereafter

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

Primary End Points: PFS, OS (RECIST 1.1 by BICR[1])

Secondary End Points: ORR, DOR, Safety, HRQoL

Additional Details: Anticipate topline readout in 2H 2024

BICR: blinded independent central review; DCR: disease control rate; HRQoL: health-related quality of life; ICR: independent central review; IHC: immunohistochemistry; RECIST: response evaluation criteria in solid tumors.
1. Response assessments until progression (per ICR or BICR) or withdrawal of consent; 2. Harding et al., Lancet Onco. 2023 24(7) 772-782; 3. CAPOX (capecitabine and oxaliplatin) or FP (5-fluorouracil and cisplatin).

Zanidatamab: Epidemiology of Biliary Tract Cancers

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]

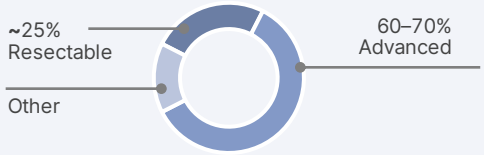
of all estimated new GBC cases occurred in Asia, with 10% (~12,570) in Europe in 2020[7]

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. * have not received FDA (or any regulat ory 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.

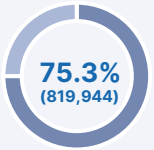
Zanidatamab: Epidemiology of Gastroesophageal Adenocarcinoma

- 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

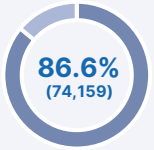
Incidence rates[11]

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

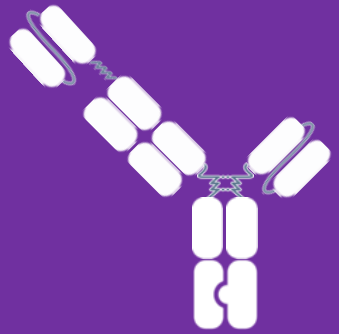
Options for patients with esophageal adenocarcinoma: ToGA (and many other HER2-directed trials in the advanced setting) excluded esophageal adenocarcinoma: in clinic, these patients can be treated with chemotherapy (capecitabine + cisplatin or fluorouracil + cisplatin) + trastuzumab in the first-line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

CPS: combined positive score; GEJ: gastroesophageal junction'; HER2+: epidermal growth factor receptor 2 positive; ITT: intention-to-treat population; mOS: median overall survival.
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.

Zanidatamab: Regulatory Designations and Exclusivity

Designation	Indications/ Patent description	Company	Territory	Status
Breakthrough therapy	BTC that has failed prior systemic therapies	BeiGene	China	Granted
Breakthrough therapy	Previously treated HER2 gene-amplified locally advanced /unresectable or metastatic BTC	Zymeworks	USA	Granted
Fast Track	HER2-overexpressing GEA (in combination with standard of care chemotherapy) and previously treated or recurrent gene-amplified BTC	Zymeworks	USA	Granted
Orphan drug	BTC	Zymeworks	USA EU	Granted
Orphan drug	Gastric Cancer HER2 expressing Gastric Cancer	Zymeworks	USA EU	Granted
Key patents	Bispecific antigen binding constructs targeting HER2	Zymeworks	USA	Granted

1. Patent end date includes certain regulatory extensions including term extensions and supplementary production certificates.



ZW171
MSLN x CD3 Multispecific

MSLN has strong expression in ovarian cancer (~84%)[2], with moderate to strong expression levels within NSCLC (~36%)[2]

Design[1]

- 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[1]

- 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.
2. Weidemann, S. et al. Biomedicines 2021, Apr 7;9(4):397.

ZW171: Designed to Widen the Therapeutic Window with Enhanced Safety and Anti-Tumor Activity

Azymetric™ and EFECT™ KO Fc

Antibody Format

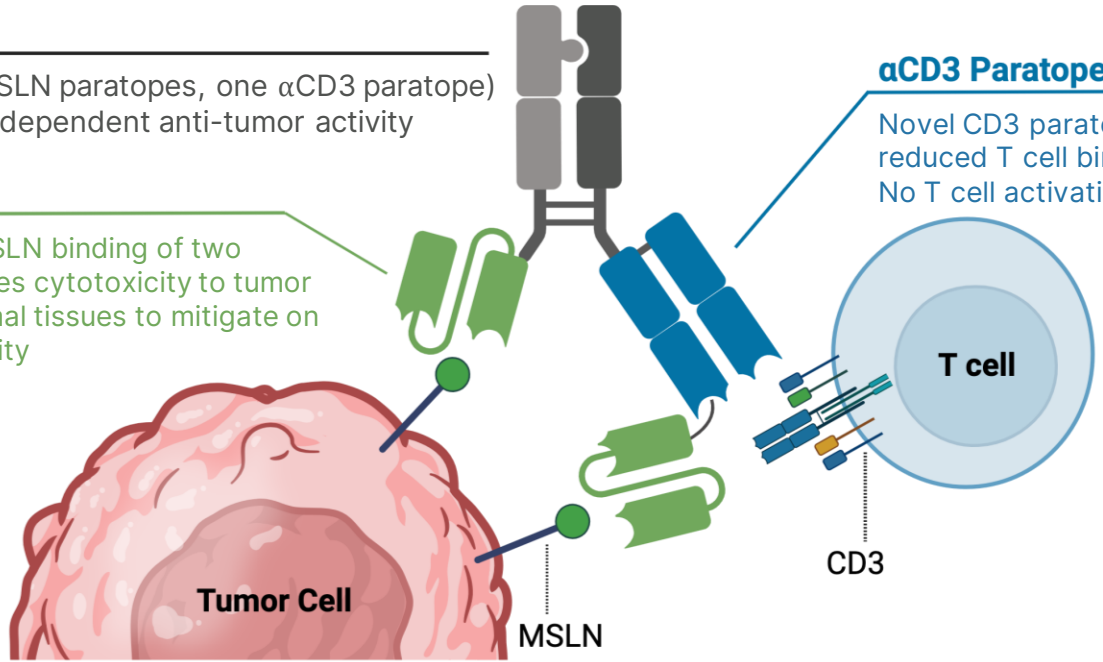
2 +1 format (two αMSLN paratopes, one αCD3 paratope) optimized for tumor-dependent anti-tumor activity

αMSLN Paratopes

Avidity dependent MSLN binding of two αMLSN paratope drives cytotoxicity to tumor cells and spares normal tissues to mitigate on target off tumor toxicity

αCD3 Paratope

Novel CD3 paratope with low affinity and reduced T cell binding designed to mitigate CRS
No T cell activation in absence of tumor



CRS: cytokine release syndrome.

ZW171: Differentiated Drug Design

Mesothelin (MSLN):

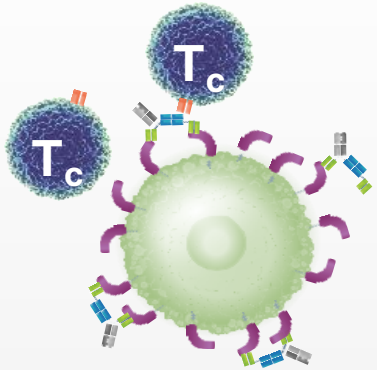
- Clinically amenable to T cell–mediated therapy (eg. Gavo-cel[1]) but limited success with other systemic therapy (e.g., ADCs,[2-4] immune toxins,[5] prior TCEs[6,7])

Designed to overcome limitations of prior targeted therapies

- Avidity-dependent MSLN binding[8]
  - Enable selective binding
  - Cytotoxicity of high/moderate MSLN-expressing cancer cells
  - Spares normal tissue
- Novel CD3 paratope[8]
  - Designed to limit cytokine release
  - Supporting effective tumor cell killing

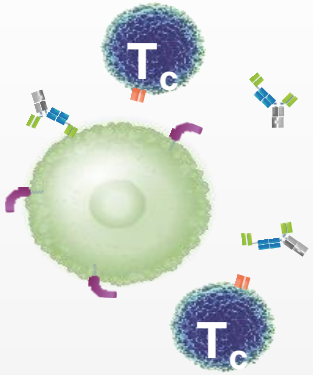
ZW171

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



ZW171 drives anti-tumor 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

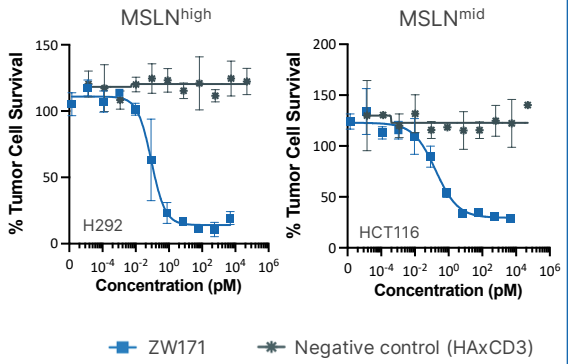
Gavo-cel: gavocabtagene autoleucel.

1. Hassan R, et al. Nat Med. 2023;29:2099-2109; 2. Kindler HL, et al. Lancet Oncol. 2022;23(4):540-552; 3. Rottey S, et al. Clin Cancer Res. 2022;28(1):95-105; 4. Weekes CD, et al. Mol Cancer Ther. 2016;15(3):439-447; 5. Hassan R, 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

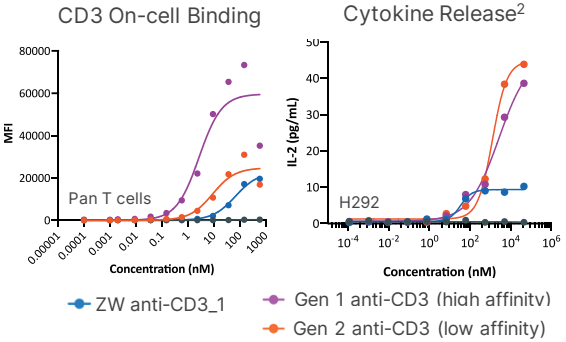
Engineered with 2+1 Format
Facilitates Avidity-Driven Binding[1]

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



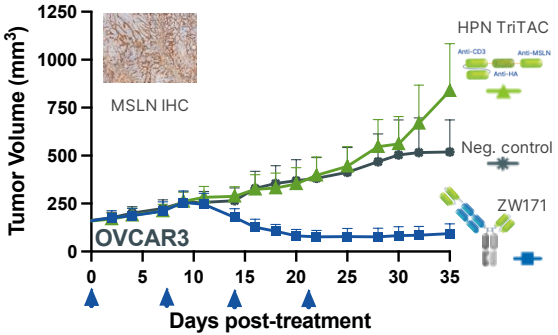
Novel CD3 Paratope with Enhanced Safety

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)

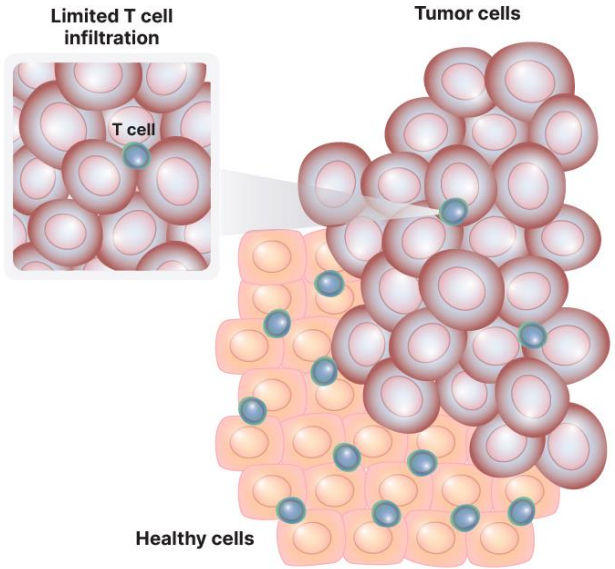
bsAb: bispecific antibody; gen: generation.
1. Afacan N et al., Abstract #2942 presented at AACR 2023; 2. Cytokine release from T cell dependent cytotoxicity assay with pan T cells and H292 tumor cells at 5:1 E:T.

Multispecific Antibody Therapeutic Development

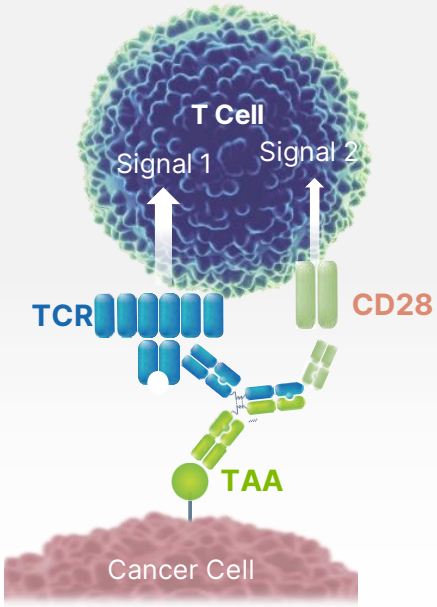
TriTCE Co-Stimulatory Therapeutic Program

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**

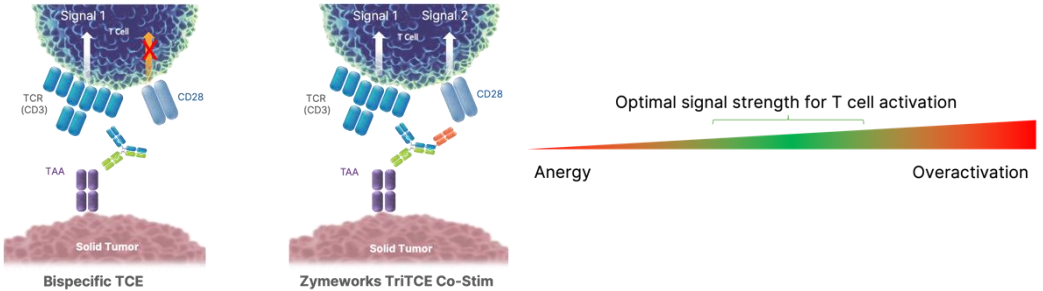
Engineered to balance signal 1 and 2 for optimized **TAA-dependent T cell activation** and expansion

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

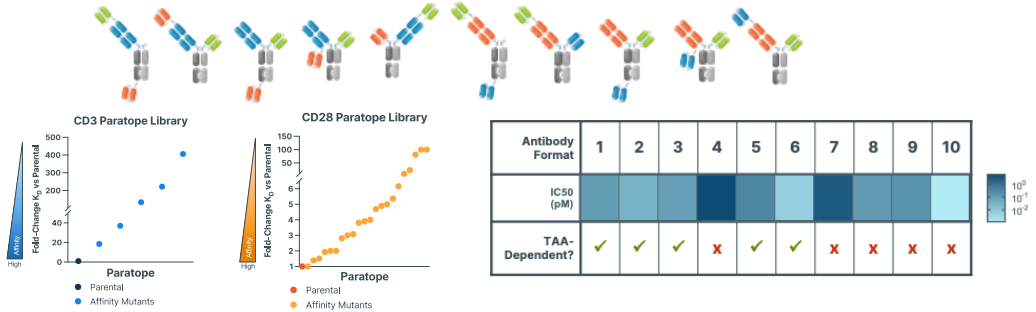
TCR: T cell receptor.
Arvedson T et al. Ann Rev Cancer Biol 2022.

Novel Engineering and Screening Approach Identifies Co-Stimulatory Trispecifics with Greater Anti-Tumor Activity and Target-Dependent T Cell Activation

Co-Stimulatory trispecific TCEs (TriTCE Co-Stim) have the potential to provide more durable responses and re-invigorate 'cold' tumors with lower T cell infiltration



Novel screening approach enables identification of optimal TriTCE format and paratope affinities for robust 'Signal 1' + 'Signal 2' T cell activation and synapse formation



Antibody Format	1	2	3	4	5	6	7	8	9	10
IC50 (pM)										
TAA-Dependent?	✓	✓	✓	x	✓	✓	x	x	x	x

10^{0}
10^{-1}
10^{-2}

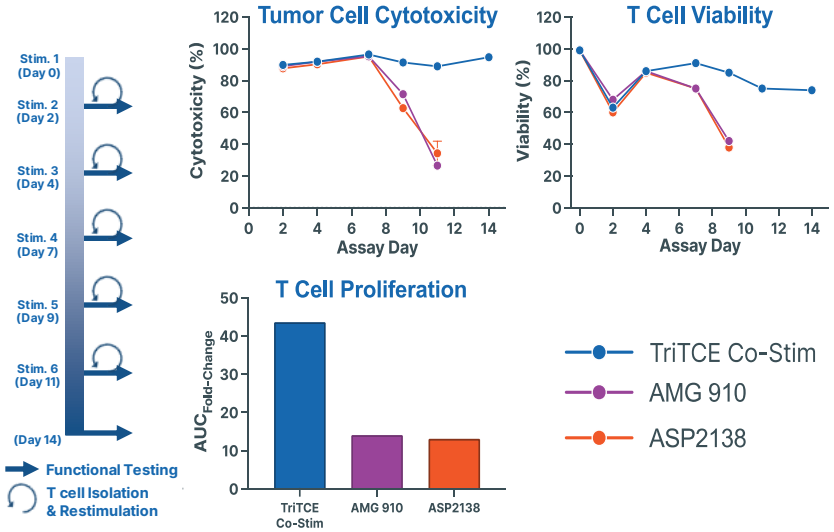
- **Engineering solutions employed to optimize signal strength** for T cell activation and anti-tumor activity, including modifications to paratope affinities and antibody format geometries
- In vitro screening identified TriTCE Co-Stim molecules with **enhanced TAA-dependent anti-tumor activity compared to a bispecific TCE**, and transferability across TAA targets

Newhook L et al., TriTCE Co-Stim, next generation costimulatory trispecific T cell engagers for the treatment of solid tumors. Abstract #5121 presented at American Association for Cancer Research annual meeting 2023.

TriTCE Co-Stim: A Next Generation Trispecific T Cell Engager Platform

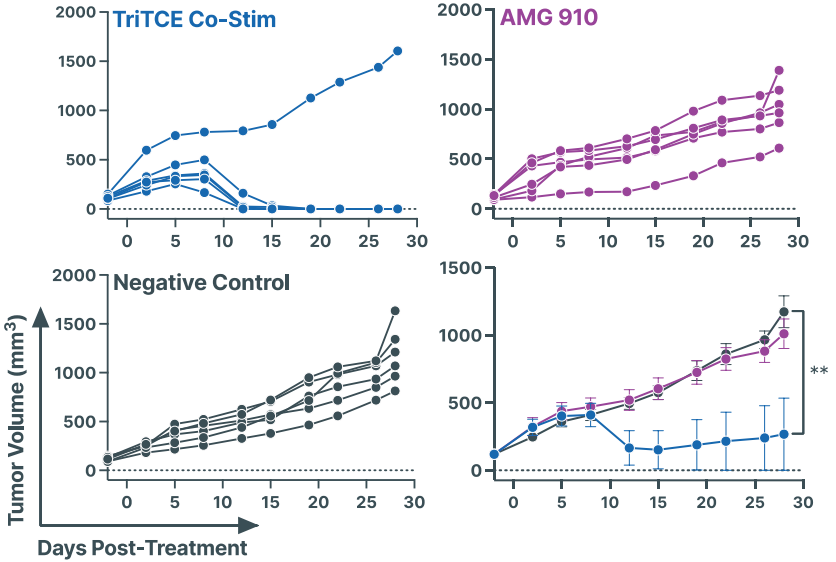
- Designed to enhance T cell activity and provide more durable anti-tumor control
- CLDN 18.2 used as a model tumor antigen and activity benchmarked against clinical stage bispecifc TCEs

Sustained T cell Cytotoxicity and T cell Fitness



CLDN18.2 TriTCE Co-Stim displays sustained T cell fitness and anti-tumor activity in a serial, repeat challenge assay. T cells were stimulated with SNU 601 cells (**5:1 E:T**) and test article (1 nM). For each subsequent round of stimulation, T cells are isolated from the T cell:tumor cell co-culture, counted, and re-stimulated with fresh SNU 601 target cells (5:1 E:T) and fresh test article (1 nM). Schematic of T cell restimulation. Following each round of stimulation, T cell: tumor cell co-cultures were assessed for tumor cell cytotoxicity, T cell viability, and T cell proliferation. Data are representative of two individual donors and are presented as mean ± SD. Insufficient T cells for continued stimulation with AMG 910 and ASP2138 following stimulation 5. Viability and proliferation data for AMG 910 and ASP2138 were excluded for stimulation 5 due to technical error (tumor cell carryover).

Enhanced Anti-Tumor Activity in Established Gastric Cancer Humanized Xenograft Model



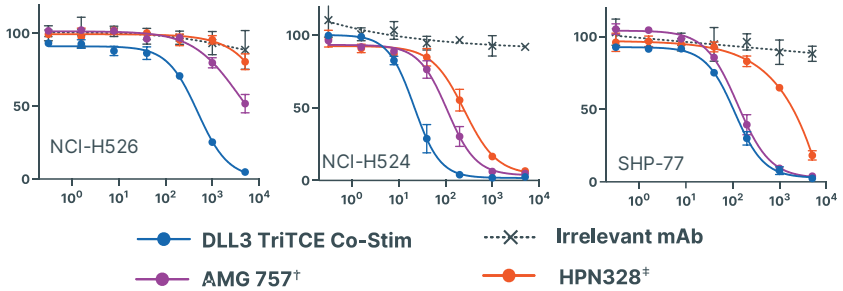
In vivo efficacy following treatment with CLDN18.2 TriTCE Co-Stim. NCG mice (n=6) were injected SC with SNU 620 (gastric) target cells, engrafted with human PBMCs, and treated IV with 0.05 mg/kg of test article qTwx4. Mice were assessed for tumor volume. Data are presented as mean ± SEM. ** p<0.01

E:T: Effector to Target ratio; NCG: nude, complement deficient, gamma-irradiated; PBMC: peripheral blood mononuclear cells; SC: subcutaneous.
AMG 910 (CLDN18.2/CD3 bispecific T cell engager) & ASP2138 (CLDN18.2/CD3 2+1 bispecific antibody) replicas produced in-house.
Newhook L et al., Abstract #6719 presented at AACR Annual Meeting 2024.

DLL3 TriTCE Co-Stim: A Next Generation Trispecific T Cell Engager

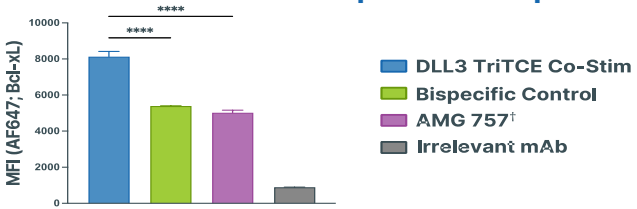
Designed to incorporate CD28 costimulation to improve activity beyond conventional DLL3xCD3 bispecifics by enhancing T cell activity and providing more durable responses in poorly infiltrated 'cold' tumors

Enhanced T Cell Cytotoxicity (SCLC)



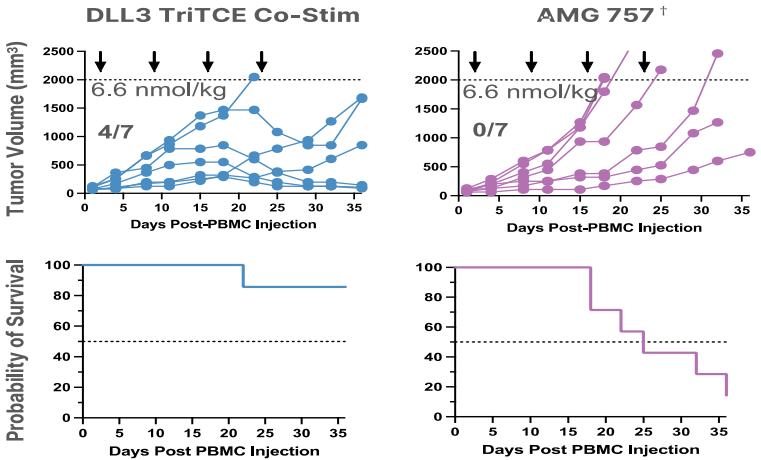
DLL3 TriTCE Co-Stim displays superior in vitro cytotoxicity relative to clinical benchmarks across multiple DLL3-positive SCLC tumor cell lines. Test articles were incubated with T cells co-cultured with DLL3-expressing tumor cell lines (E:T =1:2) for 7 days and evaluated for cytotoxicity.

Improved T Cell Survival Compared To Bispecific TCEs



DLL3 TriTCE Co-Stim Increases T cell proliferation and upregulation of anti-apoptotic marker Bcl-xL. Test articles (5 nM) were incubated with T cells co-cultured with NCI-H82 cells for 48 hours and evaluated for Bcl-xL expression by flow cytometry. **** p<0.0001

Superior Anti-tumor Activity in Established SCLC Humanized Xenograft Model



DLL3 TriTCE Co-Stim efficacy in vivo. SHP-77 cells were injected s.c. in NCG mice. Following PBMC humanization, mice were treated IV with test article q1w x 4. Tumor volume over time of mice treated with DLL3 TriTCE Co-Stim (6.6 nmol/kg), AMG 757 (6.6 nmol/kg). Full or partial tumor regression was observed in 4/7 mice treated with DLL3 TriTCE Co-Stim. Arrows indicate treatment days. Kaplan-Meier curves showing probability of survival of tumor-bearing mice treated with DLL3 TriTCE Co-Stim (blue), AMG 757 (purple, MS = 25 days). Death events represent euthanized animals due to reaching experimental endpoint (TV ≥ 2000 mm3).

SCLC: small cell lung cancer.
† AMG 757 (DLL3/CD3 bispecific t cell engager) produced in-house.
Repenning P et al., Abstract #6716 Presented at AACR Annual Meeting 2024.

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

Co-Stimulatory (CD28) TCE Strategies	Zymeworks' Potential Advantage and Limitations of Alternative Strategies
Zymeworks TriTCE Co-Stim	✓ Zymeworks TriTCE Co-Stim provides **balanced CD3 and CD28 activation** to prevent overactivation of T cells[1,2] ✓ **Tumor Target-dependent activity** associated with sustained T cell viability and cytotoxicity resulting in improved anti-tumor activity in preclinical models compared to bispecific TCEs[1,2,3,4,5] ✓ **No CD28 binding in absence of CD3 engagement**, lowering risk of CD28-mediated immune related adverse events (irAEs), well tolerated in both in vivo CRS models[1,2] and in non-human primates[3]
CD28xTAA Bispecific (e.g. Regeneron, Xencor)	❑ Optimized for strong CD28 agonism, potentially difficult to optimize by dose adjustment[6,7] ❑ Dependent on presence of signal 1 primed T cells in TME[6,7] ❑ Potential for severe irAEs in combination with anti-PD-1, similar to CPI toxicities[8,9,10,11,12]
CD3xTAA + CD28xTAA Bispecific Combinations (e.g. Regeneron, Janssen, Roche)	❑ Increased development and challenging dose optimization requirements for two molecules[13] ❑ Potential for CD28 bispecific irAEs[9] ❑ Challenging TAA pairs or non-overlapping epitope targets requirements[6]
CD28xCD3xTAA Trispecific (Sanofi)	❑ High affinity CD3 and CD28 paratopes, activation of peripheral T cells[14,15] ❑ T cell binding and TMDD observed in the periphery[14,15] ❑ CD28 paratope based on CD28 super-agonist, potentially limiting application[14,15]

CPI: checkpoint inhibitor; PD-1: programmed cell death protein 1; TMDD: tumor mediated drug disposition; TME: tumor microenvironment.

1. Newhook et al., Cancer Res. (2023); 2. Newhook et al., JITC (2023); 3. Newhook L et al., Abstract #6719 presented at AACR Annual Meeting 2024; 4. Repenning P et al., Abstract #6716 Presented at AACR Annual Meeting 2024. 5. Newhook et al., SITC (2023); 6. Skokos et al., Sci. Transl. Med. (2020); 7. Dragovich et al., Cancer Research (2023); 8. Stein et al., Journal Clinical Oncology (2023); 9. Martins et al., Nature Reviews Clin Oncol (2019); 10. Eastwood et al., BJP (2010); 11. Roemer et al., Blood (2011); 12. Hui et al., Science (2017); 13. Humphrey et al. (2011) J Natl Cancer Inst. 14. Seung et al., Nature (2022); 15. Promsote et al., Nature Communications (2023).

Next Generation CD28 Co-Stimulatory Trispecific T cell Engager

Designed to provide more durable responses in solid tumors and superior activity in ‘cold’ tumors

Therapeutic Rationale

- Next Gen TriTCE Co-Stim can provide increased T cell fitness, activation, and proliferation via tumor-dependent T cell co-stimulation

Product Differentiation

- Novel approach of modular geometry and avidity screening of trispecifics to optimize T cell activation by Signal 1 and Signal 2
- TriTCE Co-Stim show superior anti-tumor activity to bispecific benchmarks and exhibit no activation of T cells in absence of tumor cells

Next Milestones

- IND candidate nomination expected in 2H 2024
- Potential to expand utility to additional tumor targets

Expansion of R&D Strategy Beyond "5x5"

Long-Term R&D Strategy ("ADVANCE")

- 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 immune modulators

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

ADVANCE Portfolio Framework

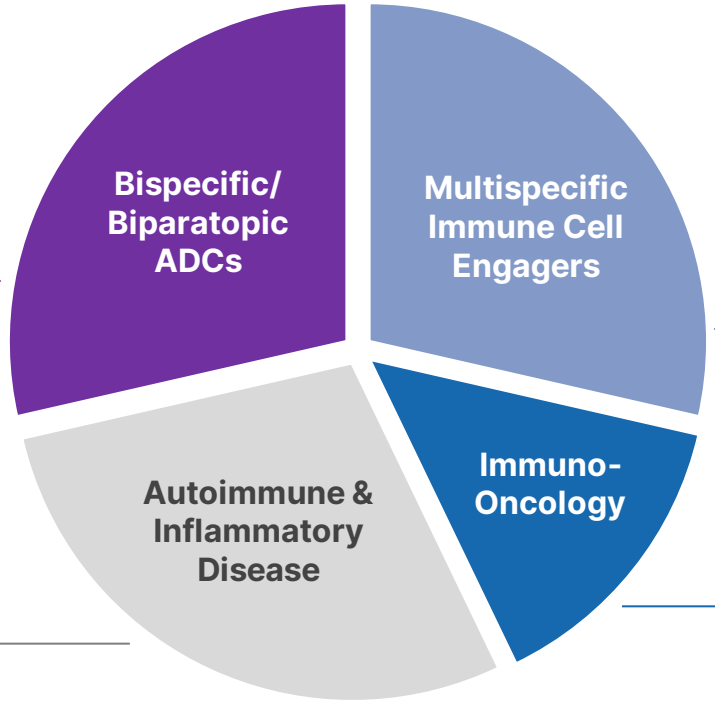
Advancing design of ADCs and Multispecifics to address complex disease states
Continue to apply technology to hard-to-treat cancers and expand utility to additional therapeutic applications

ADCs

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

AIID

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



Multispecific 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.

Milestone Opportunities in 2024 & 2025

Cash resources* as of March 31, 2024 **$420.5M**

Several opportunities for business development with unencumbered global rights for novel compounds

Current cash runway projected to support development goals into the **second half of 2027.**

Multiple value generating opportunities expected in 2024 and 2025, with **5 IND submissions expected by 2026**

Potential to nominate 2 candidates every year from 2027+

- **Top-line data from HERIZON-GEA-01** targeted for late 2024
- **Potential U.S. and China approval** for zanidatamab in 2L BTC during or before 2025

*includes cash, cash equivalents and marketable securities.

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