zymeworks

Making a Meaningful Difference

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

Nasdaq: ZYME | zymeworks.com

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This presentation includes “forward-looking statements” within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and “forward-looking information” within the meaning of Canadian securities laws, or collectively, forward-looking statements. Forward-looking statements in this press release include, but are not limited to, statements that relate to Zymeworks’ expectations regarding implementation of its corporate goals, Zymeworks’ clinical development of its product candidates, related clinical trials, anticipated clinical data presentations and the timing thereof, potential therapeutic effects of zanidatamab and its other product candidates, expected benefits of the new executive leadership team of Zymeworks, expected financial performance and future financial position, the commercial potential of technology platforms and product candidates, anticipated continued receipt of revenue from existing and future partners, Zymeworks’ preclinical pipeline, anticipated sufficiency of cash resources and other potential sources of cash to fund Zymeworks’ planned operations through at least 2026 and potentially beyond, Zymeworks’ ability to execute new collaborations and partnerships and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as “future,” “potential,” “progress,” “subject to,” “anticipate,” “plan,” “expect,” “estimate,” “project,” “may,” “will,” “could,” “can,” the negatives thereof, variations thereon and similar expressions, or by discussions of strategy. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements, including, without limitation, Zymeworks’ examination of historical operating trends, are based upon our current expectations and various assumptions. Zymeworks believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Zymeworks may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various factors, including, without limitation: the impact of the COVID-19 pandemic on Zymeworks’ business, research and clinical development plans and timelines and results of operations, including impact on its clinical trial sites, collaborators, and contractors who act for or on Zymeworks’ behalf, may be more severe and more prolonged than currently anticipated; clinical trials may not demonstrate safety and efficacy of any of Zymeworks’ or its collaborators’ product candidates; any of Zymeworks’ or its partners’ product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions; Zymeworks’ assumptions regarding its financial condition or future financial performance may be incorrect; Zymeworks may not recognize the anticipated cost savings of its reduction in workforce; inability to maintain or enter into new partnerships or strategic collaborations; and the factors described under "Risk Factors" in Zymeworks’ quarterly and annual reports and other sections of our public filings with the Securities and Exchange Commission and Canadian securities regulators.

These forward-looking statements are made only as of the date hereof, and Zymeworks Inc. undertakes no obligation to update or revise the forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Key Expected R&D Developments in 2024 and 2025

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

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

Projected Cash Runway Supports Current Strategy Through 2026 and Potentially Beyond

Updated Financial Guidance:

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

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

Potential sources to extend cash runway:

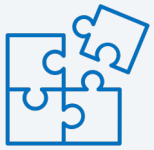
- Royalty income and commercial milestones from zanidatamab sales by Jazz and BeiGene
- Additional payments from legacy technology platform collaborations
- New partnerships/collaborations to provide upfront payments and committed R&D funding

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

Multifunctional Antibody Therapeutics for Oncology (and Beyond)

Focus on Cancer Indications with Greatest Unmet Patient Need

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



Integrated R&D Engine

Customized antibodies through in-house protein engineering and proprietary technology

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

Desired Product Profile

First and second-line market opportunities

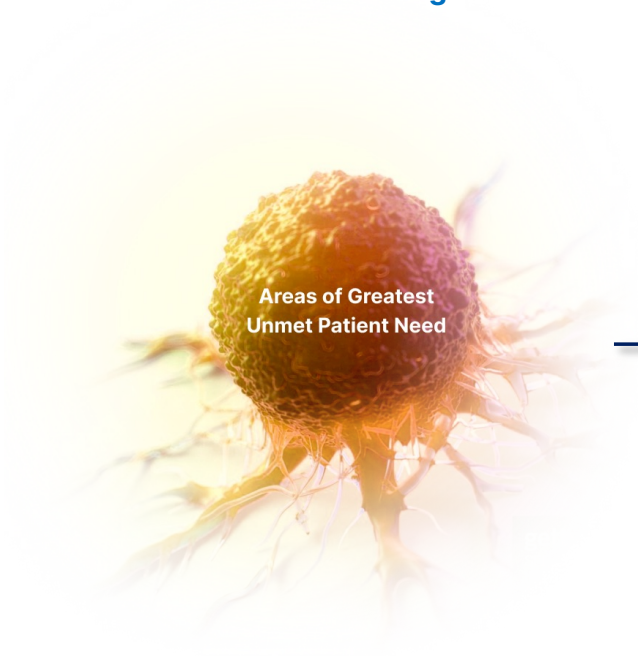
Pursuing lead indications with global peak sales potential >$1 B

Strategy to retain US commercial rights

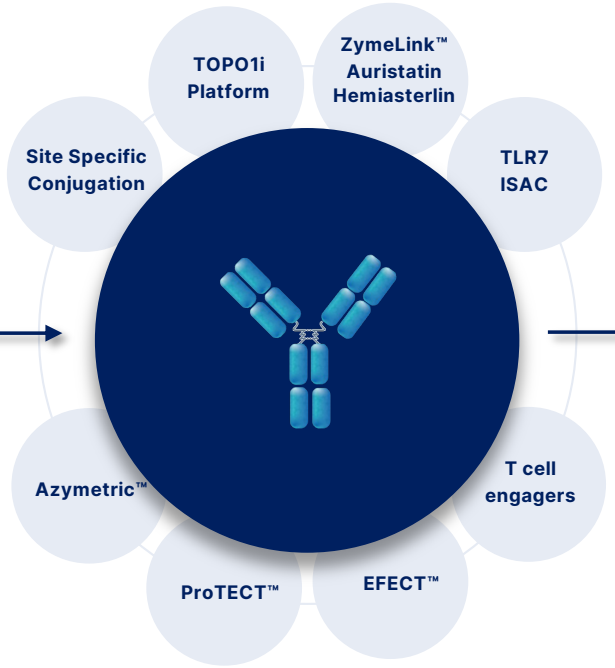
OS: overall survival
1.Combinable proprietary technologies include: Azymetric; EFECT; ProTECT; ADC Platform includes cysteine insertion technology and novel payloads

ADC and Multispecific Modalities Driving Our Pipeline

Select Difficult-to-Treat Cancers & Target

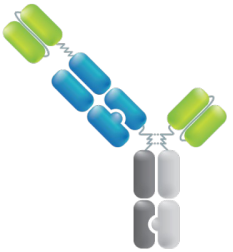


Design with Complementary Technology



Optionality with Two Foundational Fit-for-Purpose Modalities

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



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

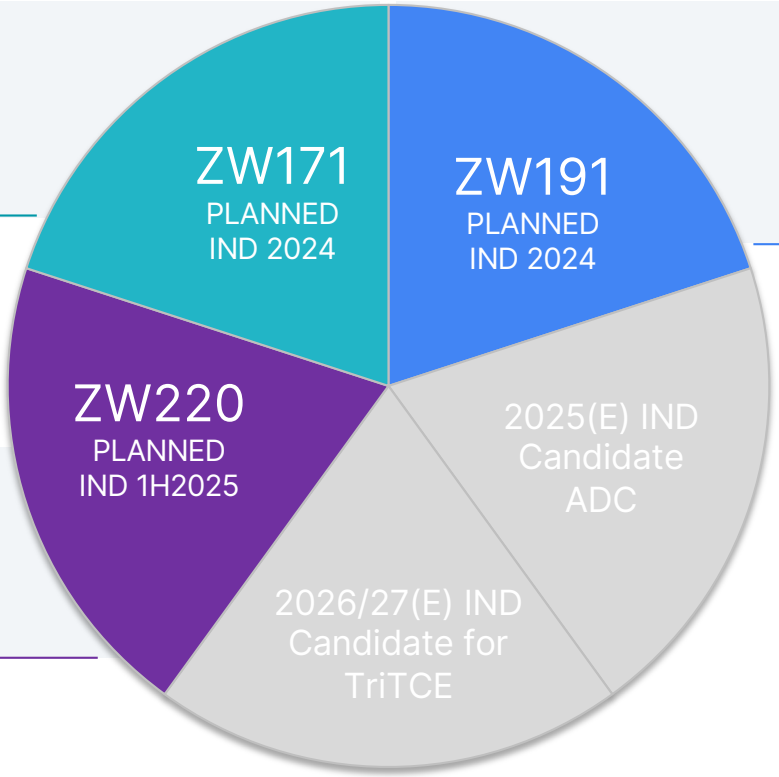
Goal of 5 **New** INDs by 2027

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

"5x5" R&D Strategy: Portfolio Construction

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

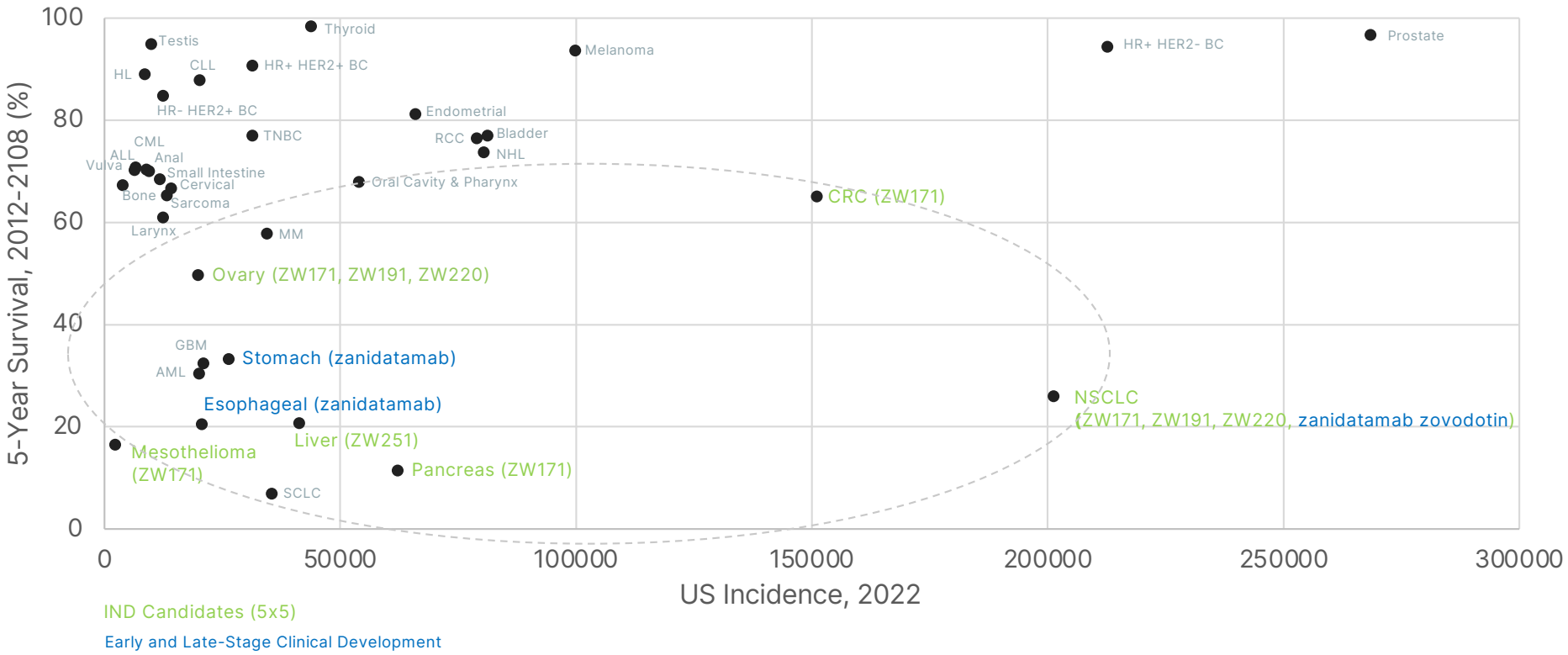
ZW191
Antibody Drug Conjugate
targeting folate receptor alpha expressing tumors including ovarian, other gynecological, and non-small cell lung cancers



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

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

Focus on Cancers With Highest Unmet Medical Need



SEER*Explorer, accessed 10 Oct 2022

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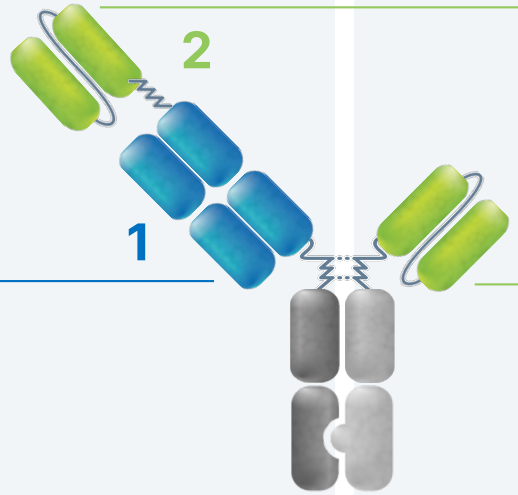
Multispecific Antibody Therapeutic (MSAT) Program

Multispecific Antibody Therapeutics Development

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

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

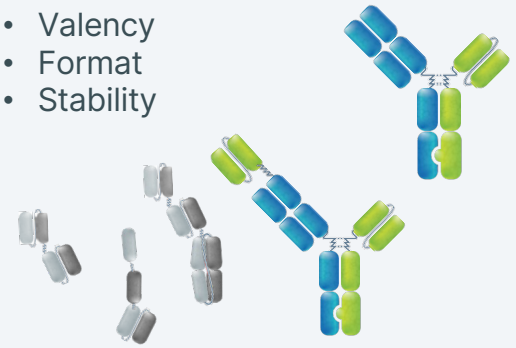


e.g., ZW171

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

3

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

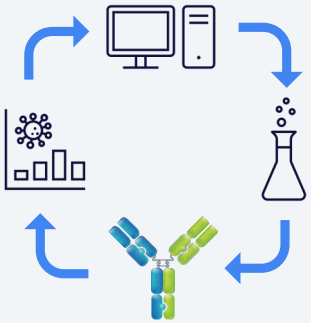


T cell engager antibody design is critical for a **widened therapeutic index** and **optimal T cell synapse formation**

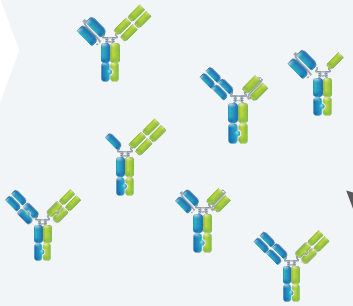
TAA: tumor associated antigen; TCE: t cell engager

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

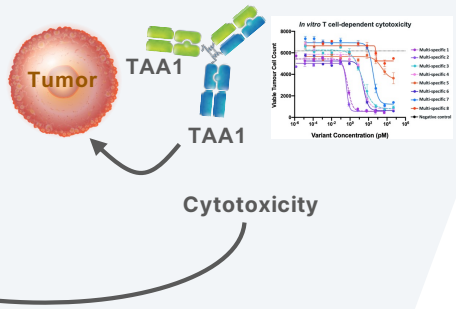
Paratope screening & optimization, *in silico* affinity engineering



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



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



Single lead optimized to:

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

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

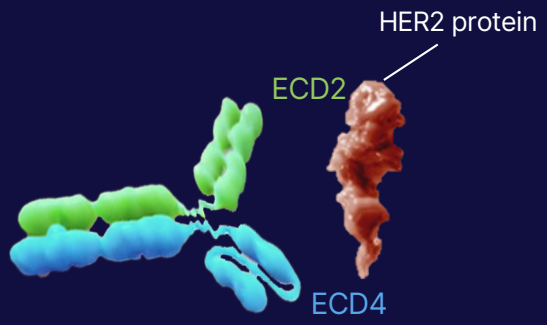
TAA: tumor associated antigen

Differentiated Development of Multi-Specific Antibody Therapeutics

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

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

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



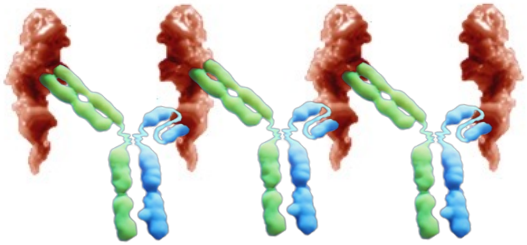
Zanidatamab

A Bispecific Antibody for HER2-Expressing Cancers

Zanidatamab's Unique Format Promotes:

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

Biparatopic HER2-Binding of Zanidatamab Drives Multiple Mechanisms of Action



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

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

ADCC: antibody-dependent cellular cytotoxicity; ADCP: antibody-dependent cellular phagocytosis; CDC: complement-dependent cytotoxicity; ECD: extracellular domain; Fc: fragment crystallizable region of antibody; HER2: human epidermal growth factor receptor 2

1.Weisser N et al., Nature Communications 2023

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

Clinical Data

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

Single Agent Activity in Second-Line BTC

- 41.3% ORR, 12.9 months mDoR[1]

Combination Activity in First-Line GEA

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

Pivotal Trials

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

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

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

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

Expected Catalysts

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

Collaboration Partners:

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

Key Financial Terms of Licensing Agreement with Jazz

	Licensing Agreement Terms[1]
Counterparty	Jazz Pharmaceuticals
Upfront Payments	$375,000,000 received in 4Q22
Regulatory Milestones	Up to $525,000,000
Commercial Milestones	Up to $862,500,000
Royalties	Tiered royalties of 10 to 20% of net sales
Current R&D Spend	All costs for ongoing clinical studies to be reimbursed 100% by Jazz[2]
Territories	US, EU, Japan and all other territories except those in Asia Pacific not covered by BeiGene agreement
Future R&D Spend	Jazz to fund 100% of costs of future studies

Key Benefits to Zanidatamab Licensing Agreement:

- **Meaningful improvement to financial position and reduction in future expenditures** allows focus on growth of exciting early-stage pipeline while zanidatamab advances to commercialization
- **Accelerate** and **expand R&D programs** (early R&D and zani zo) while maintaining anticipated cash runway through at least 2026 with a goal of advancing ***5 new programs into clinical studies in 5 years***
- **Continued management** of existing zanidatamab program by Zymeworks, in partnership with Jazz, including first BLA, **leveraging existing internal expertise to progress programs rapidly**, with future zanidatamab-related clinical studies, regulatory filings, and commercialization to be managed and funded by Jazz
- **Substantial potential milestone payments** based on global regulatory milestones for zanidatamab in BTC and GEA with further upside from royalties and commercial milestones
- **Leverage** Jazz's global commercial infrastructure together with BeiGene's complementary strengths in APAC regions to **optimize commercialization of zanidatamab without requirement for investment in commercial infrastructure** within Zymeworks

APAC: Asia Pacific; BTC: bilary tract cancers; GEA: gastroesophageal adenocarcinoma

[1] All dollar values in US Dollars; [2] Costs related to ongoing clinical studies incurred after signing of the agreement to be reimbursed 100% by Jazz, includes approximately $24M in reimbursable amounts from 4Q22

Key Financial Terms of Asia Pacific Licensing Agreement with BeiGene

	Licensing Agreement Terms[1]
Counterparty	BeiGene
Upfront Payments	$40,000,000
Development and Commercial Milestones	Up to $195,000,000
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 $40MM upfront payment in 2018 and $20MM 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

Advancing 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 median PFS 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 = 714

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 2024

BICR: Blind independent central review; BTC: Bilary Tract Cancer; DCR: Disease control rate; DOR: Duration of response; GEA: gastroesophageal adenocarcinoma; HRQoL: Health-related quality of life; ICR: Independent central review; IHC: Immunohistochemistry; PFS: Progression-free survival; OS: overall survival; 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]SOC: standard of care (chemotherapy: CAPOX or FP)

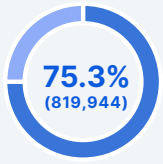
Epidemiology of GEA

- GEA is a term that 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

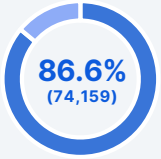
Incidence rates[11]

US	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]

US	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]

HER2+, epidermal growth factor receptor 2 positive

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

Targeted Treatment Options For Patients with HER2+ GEA

FIRST-LINE HER2+ TREATMENT OPTIONS

Advanced / Metastatic HER2+ Gastric or GEJ Adenocarcinoma

Guideline[2,3] 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

Advanced / Metastatic HER2+ Gastric or GEJ Adenocarcinoma

Guideline[2,3] option based on Keynote 811 trial[5,6]

Doublet chemo (fluoropyrimidine & platinum)+trastuzumab
±pembrolizumab

ORR = 74.4 vs 51.9%
mDOR = 10.6 vs 9.5 months
mPFS = not reported
mOS = not reported

ToGA[4] (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]

GEA, gastroesophageal adenocarcinoma; GEJ, gastroesophageal junction'; HER2+, epidermal growth factor receptor 2 positive; mDOR median duration of response; mOS median overall survival; mPFS, median progression free survival; mORR, median overall response rate

1. Catenacci et al., ESMO Open 2022 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. Keytruda (pembrolizumab): USPI 2021. 6. Janjigian YY et al. J Clin Onc 2021

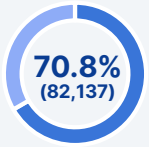
Epidemiology of Biliary Tract Cancer

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]



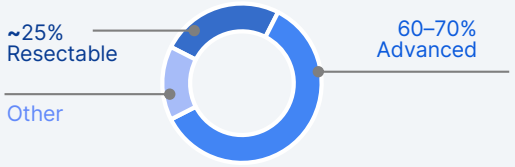
of all estimated new GBC cases occurred in Asia, with 10% (~12,570) in Europe in 2020[7]

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 1L treatment is modest, ~35% of patients get 2L, but it ranges by geographical region[11, 12, 13]
- 2L chemotherapy yields response rates of < 10%; median overall survival 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]

1L, first line; 2L, second line; HER2, human epidermal growth factor receptor 2

1.Bogenberger JM et al., Precision Oncol. 2018; 2.Lazcano-Ponce EC et al., CA: Cancer J Clin. 2001; 3. Ouyang GMM 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

Targeted Treatment Options for Patients are Rapidly Evolving in Biliary Tract Cancer

Actionable driver mutations have been identified and are generally mutually exclusive from one another (including FGFR pathway, IDH1, BRAF, NTRK, ERBB2 (HER2) MSI-high or MMR deficiency)[1]

Advanced / Metastatic Biliary Tract Cancer

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%, mPFS= 7.2 months,
mOS = 12.9 months

Progression in Metastatic Biliary Tract Cancer

SECOND-LINE TREATMENT OPTIONS[2]

Guideline option from the ABC-06 trial[6]
FOLFOX ORR= 5%, mPFS= 4.0 months,
mOS = 6.2 months

Is Targeted Treatment More Effective Than Chemotherapy?

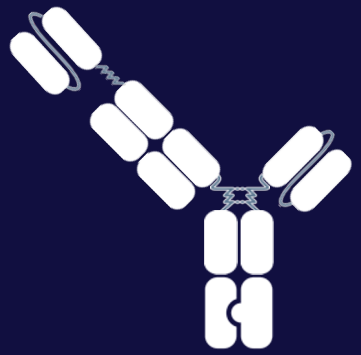
FGFR2 fusions+: mPFS= 7.0 – 9.0, mOS= 17.5 – 21.7 months[7]
IDH1 mutation: mPFS = 2.7 months, mOS = 10.3 months[8]

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

Trastuzumab + FOLFOX mPFS = 5.1 months, mOS = 10.7 months[9]
TDXd (HERB trial) mPFS = 5.1 months, mOS = 7.1 months[10]
Trastuzumab + Pertuzumab (MyPathway) mPFS = 4.0, mOS = 10.9 months[11]

1L, first line treatment; 2L, second line treatment; BRAF, activating serine/threonine-protein kinase B-raf kinase; ERBB2, receptor tyrosine-protein kinase erB-2; FGFR2 fusions+, fibroblast growth factor receptor 2 fusions and alterations; FOLFOX, folinic acid, fluorouracil, and oxaliplatin; HER2, human epidermal growth factor receptor 2; IDH1, isocitrate dehydrogenase 1; MMR, mismatch repair; mPFS, median progression-free survival; mOS, median overall survival; MSI, microsatellite instability; NTRK, neurotrophic receptor tyrosine kinase; ORR, overall response rate; SOC, standard of care; 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.Lamarca et al., J Clin Oncol 2019; 7.Vogel A et al., Annu Rev Med 2023; 8.TIBSOVO US PI Aug 2021; 9.Lee, C-K et al., Lancet Gastroenterol. Hepatol. 2023; 10.Ohba A et al., J Clin Oncol 2022 v40, no.16_suppl; 11.Javel M et al., Lancet Oncol 2021.



ZW171
MSLN x CD3 Multispecific

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

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

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

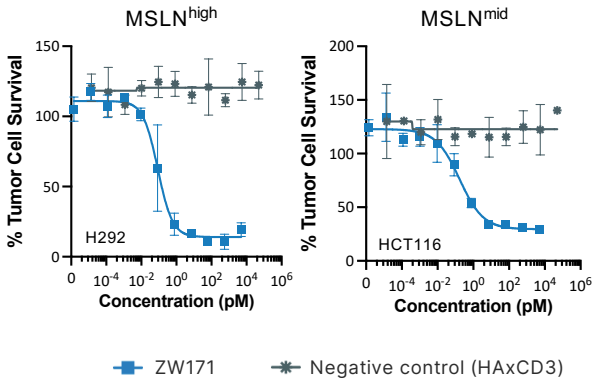
Profile
Enhanced anti-tumor activity and safety profile in preclinical models supports opportunity to overcome clinical limitations of prior MSLN-directed therapies

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

ZW171: MSLN x CD3 T-Cell Engaging Multispecific

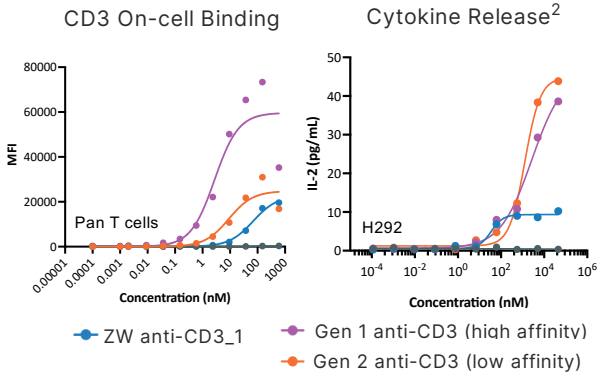
Engineered with 2+1 Format
Facilitates Avidity-Driven Binding[1]

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



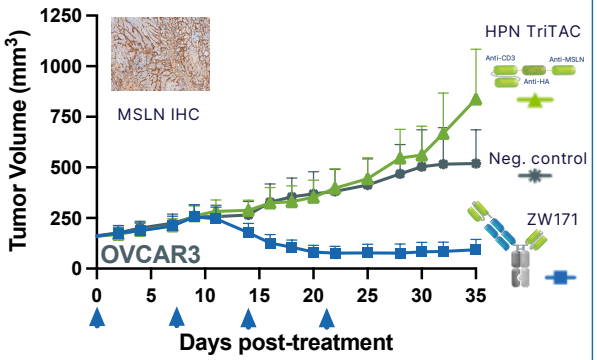
Novel CD3 Paratope with Enhanced Safety

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



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

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



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

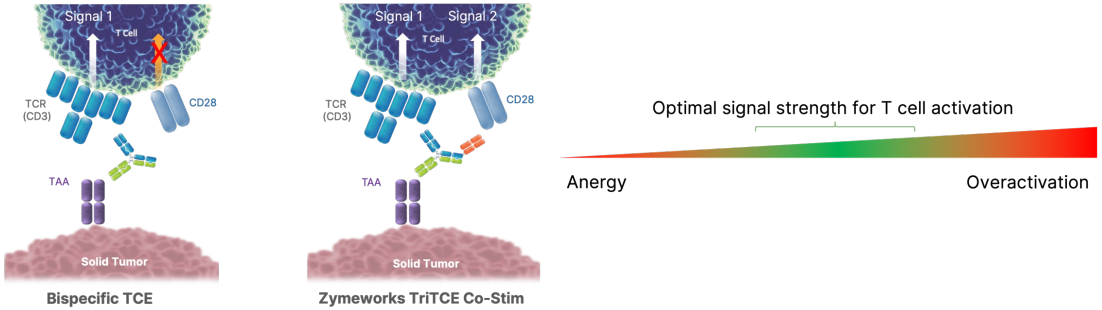
bsAb: bispecific antibody; Gen: generation; MSLN: mesothelin
1. Afacan N et al., Abstract #2942 presented at AACR 2023 2. Cytokine release from T cell dependent cytotoxicity assay with pan T cells and H292 tumor cells at 5:1 E:T

Multispecific Antibody Therapeutic Development

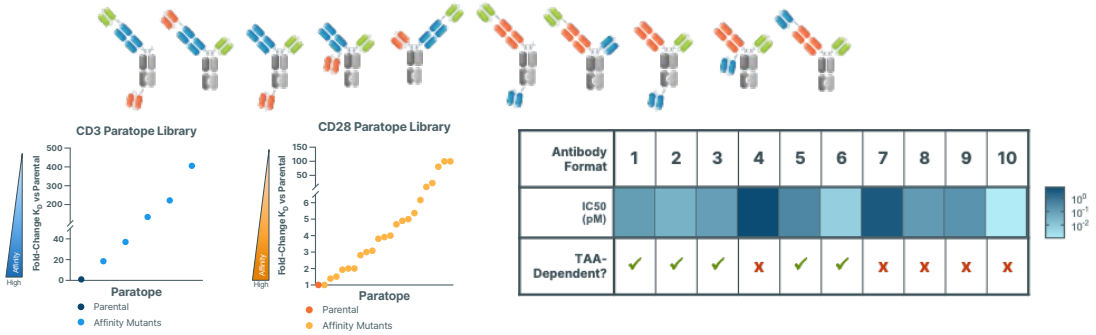
TriTCE Co-Stimulatory Therapeutic Program

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



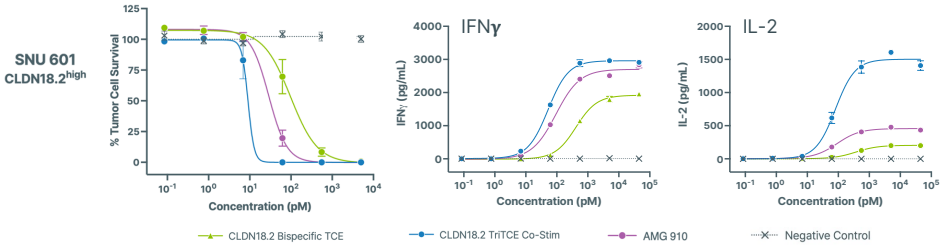
Antibody Format	1	2	3	4	5	6	7	8	9	10
IC50 (pM)										
TAA-Dependent?	✓	✓	✓	x	✓	✓	x	x	x	x

- TriTCE Co-stim have **the potential to provide more durable responses** and re-invigorate 'cold' tumors with lower T cell infiltration via tumor-dependent T cell activation (CD3) and co-stimulation (CD28)
- **Engineering solutions employed to optimize signal strength** for T cell activation and anti-tumor activity, including modifications 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.

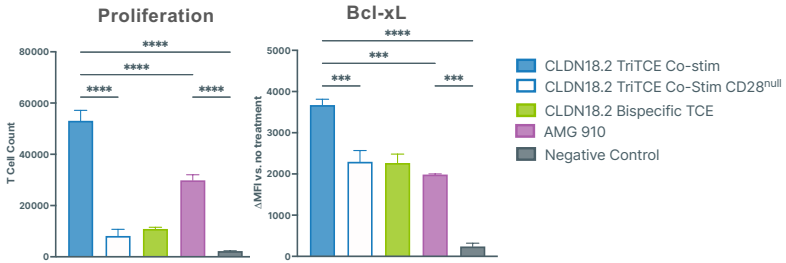
CLDN18.2 TriTCE Co-Stimulatory Molecules Mediate Enhanced in vitro and in vivo Anti-Tumor Activity Compared to Bispecific TCE

Enhanced Cytotoxicity and CD28-Dependent Cytokine Activity* at Low E:T



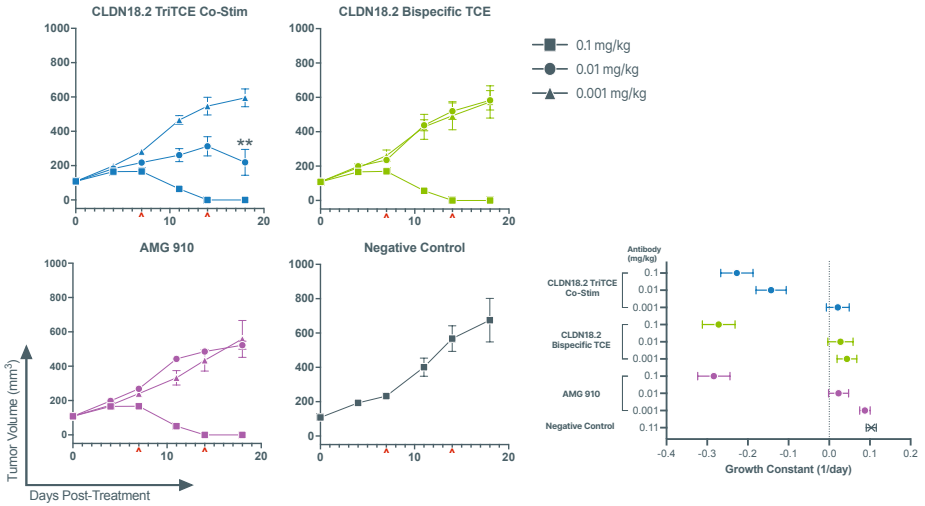
*No cytokine release observed with T-cells alone

Improved T cell Proliferation and Survival



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

Superior in vivo Anti-Tumor Activity



CLDN18.2 TriTCE molecules show enhanced TAA-dependent anti-tumor activity and T cell functionality compared to bispecific TCE

TAA: tumor-associated antigen; TCE: t cell engager

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.

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

Pilot toxicology studies and PK analyses with lead CLDN18.2 Co-stim

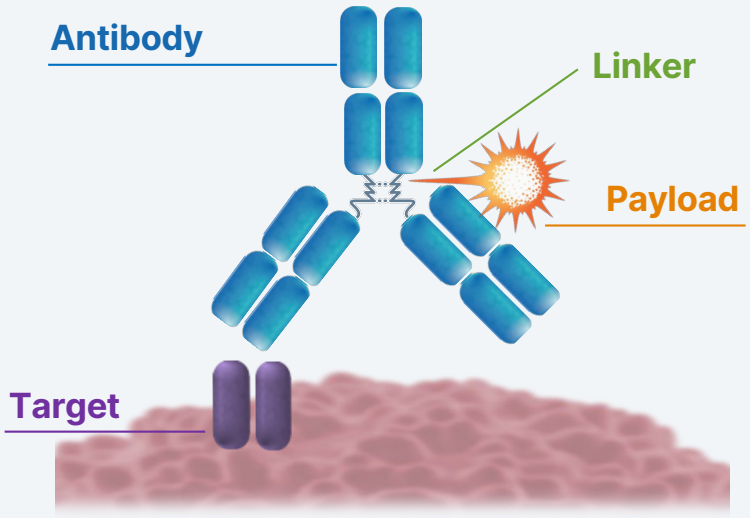
Expand utility to additional tumor targets

TCE: t cell engager; TriTCE Co-Stim: Co-stimulatory trispecific TCEs; PK: pharmacokinetics

Antibody-Drug Conjugate (ADC) Program

Building Next-Generation ADCs

Next-Generation ADCs

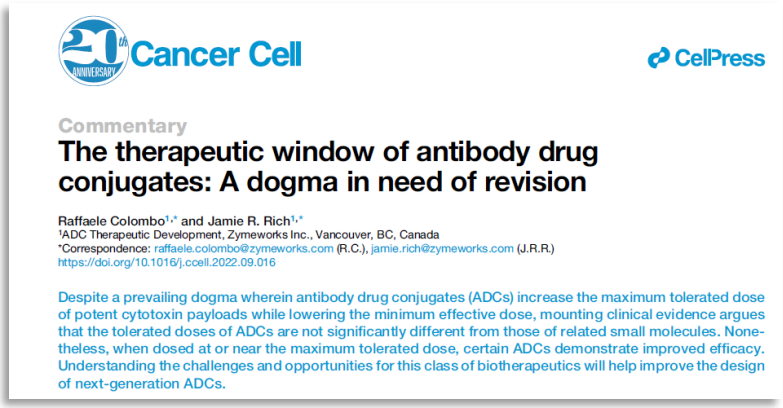


- Focusing on **validated targets** provides opportunity for benchmarking in preclinical development and expected clinical differentiation; novelty of targets anticipated to increase over time
- Exploiting our **proprietary TOPO1i payload (ZD06519)** while exploring alternate mechanisms of action for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

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

ADC: antibody drug conjugate; TOPO1i: topoisomerase 1 inhibitor
1. Colombo R, Rich JR. Cancer Cell 2022 (40)
2. Colombo R, Barnscher SD, Rich, JR. Cancer Res 2023, *83* (7). Abstract #1538 presented at AACR 2023

Platform Design Criteria Draw on Well Validated ADC Technologies



Cancer Cell

CellPress

Commentary

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

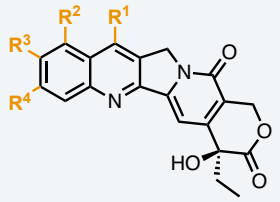
Raffaele Colombo[1,*] and Jamie R. Rich[1,*]
[1]ADC Therapeutic Development, Zymeworks Inc., Vancouver, BC, Canada
*Correspondence: raffaele.colombo@zymeworks.com (R.C.), jamie.rich@zymeworks.com (J.R.R.)
https://doi.org/10.1016/j.ccell.2022.09.016

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

Payload

Novel camptothecin with moderate potency and strong bystander activity

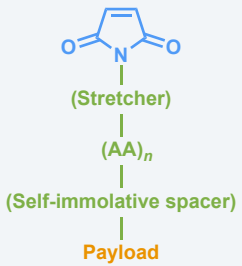
- Acknowledges complex mechanisms driving TOPO1i ADC action
- Sufficient tolerability to achieve ADC dose > 5 mg/kg



Linker

Traceless, plasma-stable, cleavable peptide

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



Conjugation

Thiol-maleimide chemistry

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

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

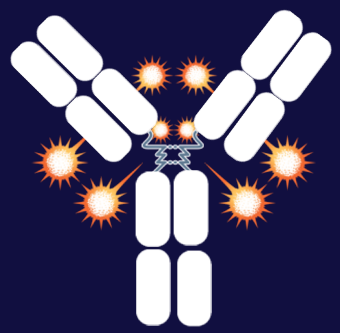
Differentiated Development of Antibody Drug Conjugates

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

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

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

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



ZW191
FRα-targeting ADC

On track for IND filing in 2024

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

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

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

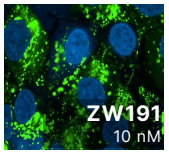
*Gyne; NSCLC; TNBC;
ADC: antibody drug conjugate; DAR: drug to antibody ratio; FRα: folate receptor alpha; IND: investigational new drug

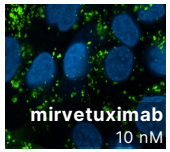
1. Lawn S et al. Abstract # 2641 Presented at AACR 2023

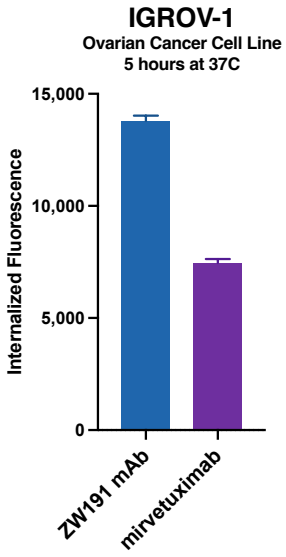
On Track for Clinical Studies in 2024: ZW191 FRα ADC

Customized format for enhanced function

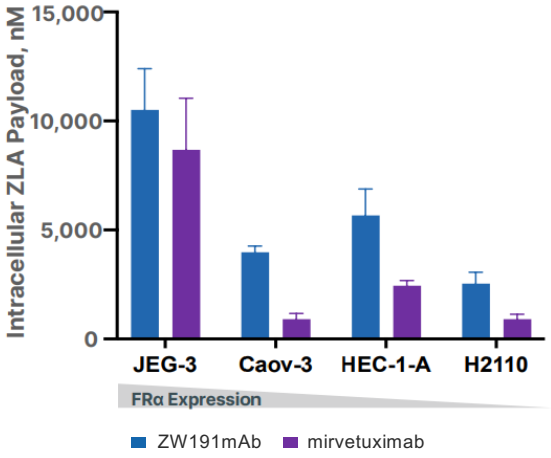
Selected for Enhanced Internalization





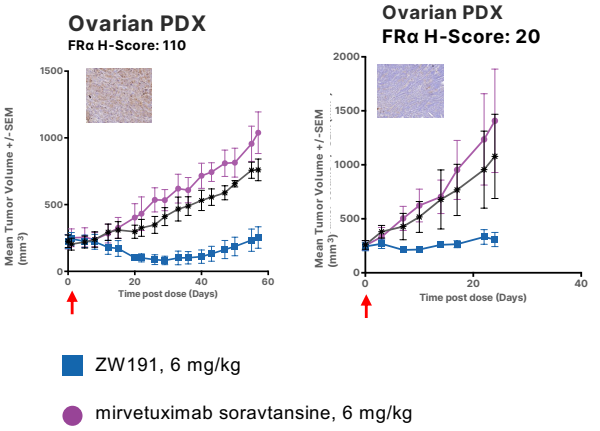


Optimized for Superior Payload Delivery



Differentiated by Greater Anti-Tumor Activity

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



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

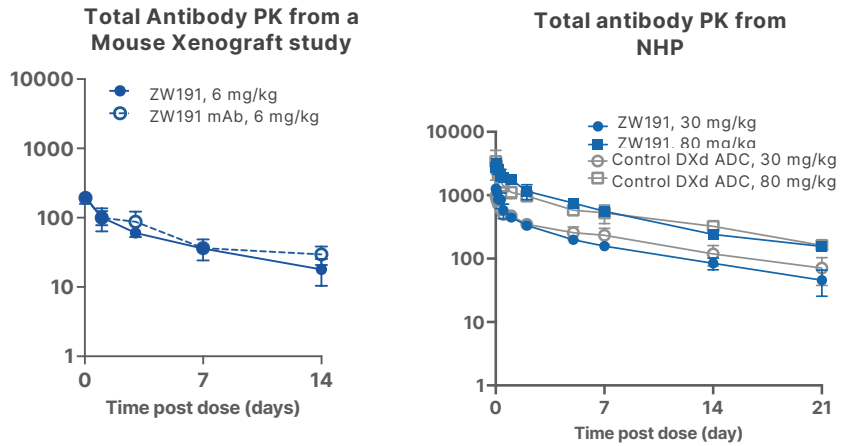
ZW191: Differentiated FRα-Targeting ADC Utilizing a Novel TOPO1i Payload

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 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 a 2024 IND

GMP: good manufacturing practices; IND: investigational new drug;; MTD: maximum tolerated dose; NHP: non-human primates; PK: pharmacokinetics

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

ZW220
NaPi2b-targeting ADC

On track for IND filing in 1H-2025

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

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

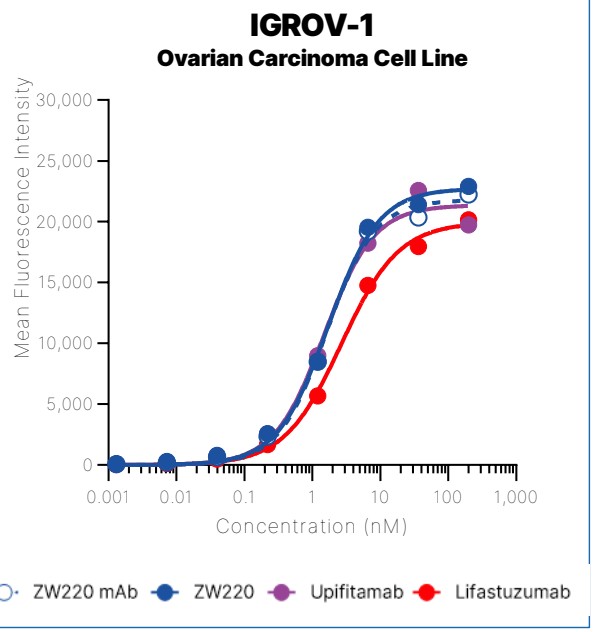
Profile
A NaPi2b ADC demonstrating activity across preclinical tumor models,[1] with first-in-class potential in ovarian and non-small cell lung cancer

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

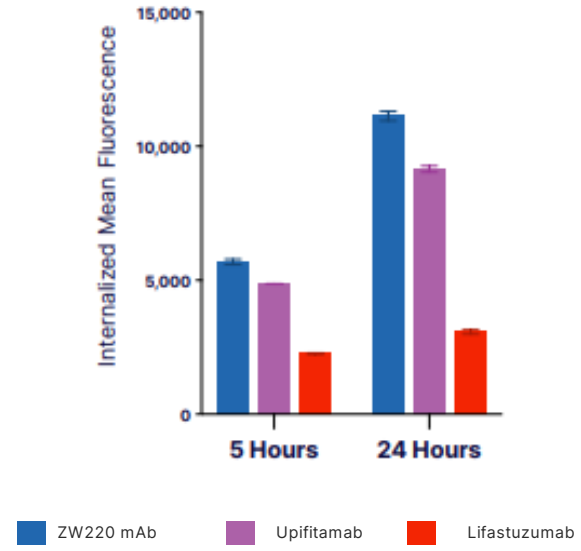
On Track for Clinical Studies in 2025: ZW220 NaPi2b-targeting ADC[1,2]

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

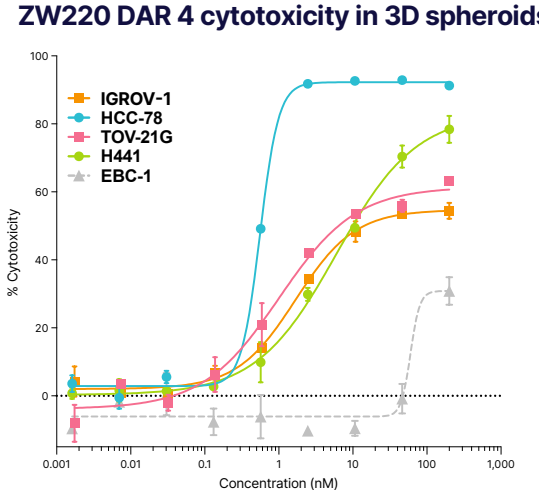
Selected for Strong Binding



Efficient & Rapid Internalization Drives Payload Delivery



Growth Inhibition in Ovarian and NSCLC Models



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

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
NaPi2b: sodium-dependent phosphate transporter; nM: nanomolar; mAb: monoclonal antibody; NSCLC: non-small cell lung cancer; PDX: patient derived xenograft
1.Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023; 2.Hernandez Rojas A et al. Presentation at World ADC 2023

ZW220 is Well-Tolerated in a Repeat Dose Non-Human Primate Toxicology Study

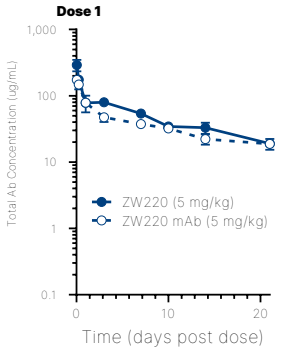
ZW220 3-dose non-GLP NHP toxicology study, Q3Wx3

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	

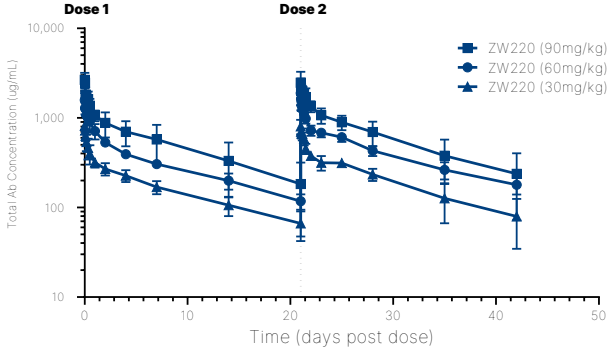
- The MTD of ZW220 in NHPs is 90 mg/kg
- No mortality or adverse pathology findings were observed at high doses

ZW220 has a Favorable Pharmacokinetic Profile

Total Antibody PK from a Tg32 Humanized FcRn Mice



Total antibody PK from NHP



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

NHP: non-human primate; GLP: good laboratory practices; MTD: maximum tolerated dose; mAb: monoclonal antibody; PK: pharmacokinetics
Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023

ZW251
Glypican 3-targeting ADC

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

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

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

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

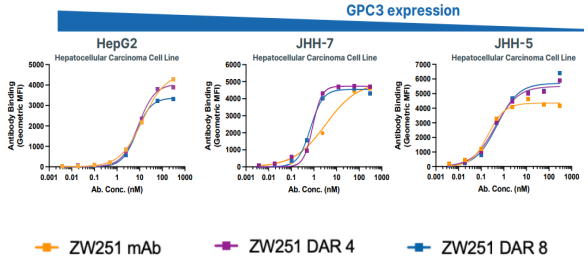
ADC: antibody drug conjugate; DAR: drug to antibody ratio; GPC3: glypican-3; HCC: hepatocellular carcinoma
1. Wang HL et al., Arch Pathol Lab Med 2008 2.Madera L et al., Abstract #2658 presented at AACR 2023

GPC3-Targeting ADC for Hepatocellular Carcinoma[1,2]

Evaluating optimal design

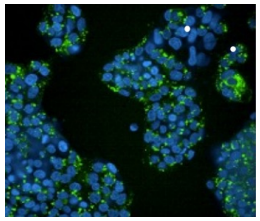
Selected for Strong Binding Across a Range of Expression Levels

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

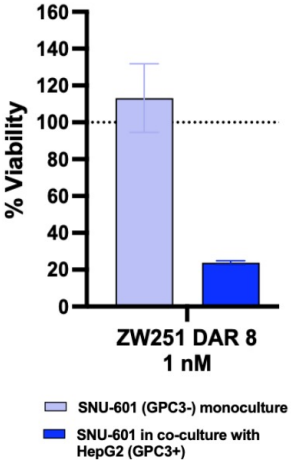


Optimized Internalization of ZW251 with Bystander Activity in Cancer Cell Co-Culture Assay

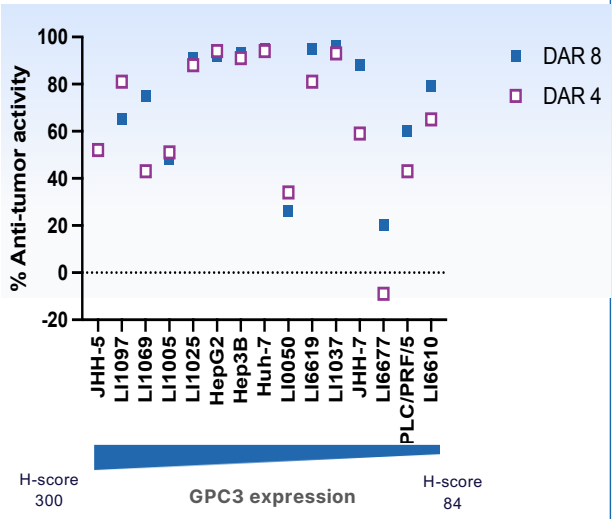
ZW251 internalized in HepG2 cell line



ZW251 Bystander Activity



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



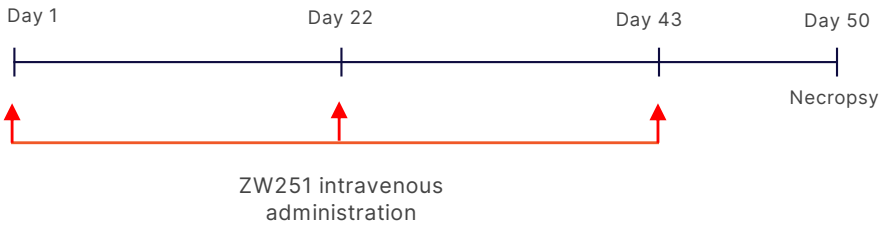
% anti-tumor activity was determined by % tumor growth inhibition (%TGI) calculated as [(1-TVtreatment/TVvehicle) x 100] at Day 21, or at the closest evaluable time point.

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

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

ZW251: Novel Glypican 3-targeting ADC Utilizing a TOPO1i Payload

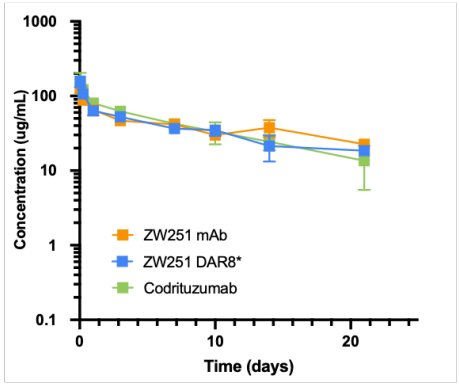
Three Dose Non-Human Primate (NHP) Toxicology Study



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

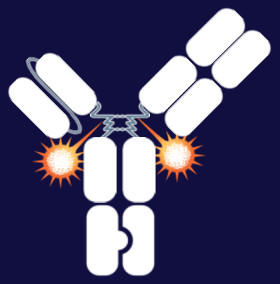


*Analog utilizes ZW251 mAb conjugated to a closely related linker-payload.

- 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)

DAR: drug-to-antibody ratio; NHP: non-human primate; mAb: monoclonal antibody; PK: pharmacokinetics

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.



Zanidatamab zovodotin

A Bispecific HER2-targeting ADC

Phase 2 expansion into NSCLC in 2023

Design

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

Mechanism

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

Profile

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

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

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

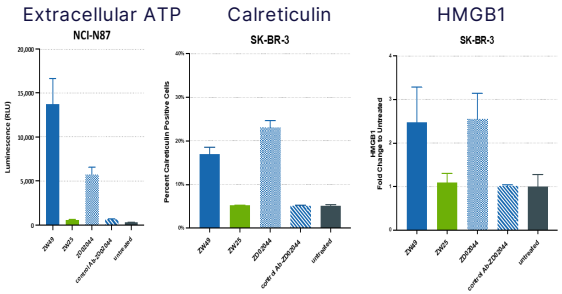
Zanidatamab Zovodotin: A Bispecific HER2-Targeting ADC

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]

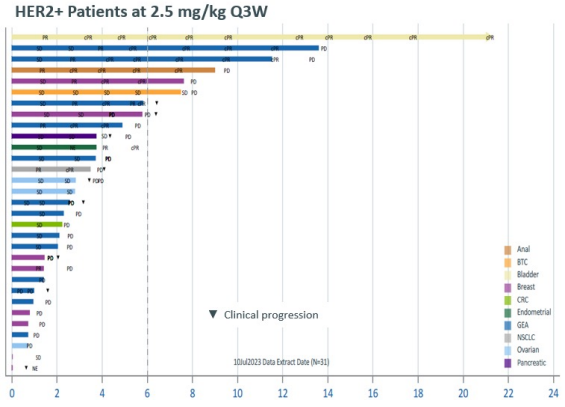
Hallmarks of ICD in HER2 expressing tumour cells



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



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

- 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

ADC: antibody drug conjugate; HER2: human epidermal growth factor receptor 2; IHMGB1, High mobility group box 1 protein; CD, immunogenic cell death; ILD: Interstitial lung disease; IRR immune related reaction; MMAE, Monomethyl auristatin E; MTD: maximum tolerated dose; NSCLC, non-small-cell lung cancer; ORR overall response rate; PK, pharmacokinetics; 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) Oh Y et al., Abstract# 33234 presented at AACR-NCI-EORTC 2023

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

R&D Strategy

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

Therapeutic Optionality

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

Financial Structure

Combination of internally-funded and partnered development programs

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

Key Events and Milestones for Remainder of 2023

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

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

Key Investment Highlights

Near-term commercialization of zanidatamab

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

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

Differentiated future product pipeline

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

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

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

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

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

Experienced Leadership Team

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

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