



Making a Meaningful Difference

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

Investor and Analyst Presentation

NOVEMBER 2024

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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 Jaz, BeiGene and other partners, including ongoing clinical studies and regulatory reviews; the conduct of an ongoing confirmatory trial to evaluate the efficacy and safety of zanidatamab; 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; 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 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
- 2L BTC (IHC3+) U.S. FDA Approval
- 1L BTC confirmatory trial ongoing
- Phase 3 GEA top-line PFS readout estimated 2Q25
- Phase 3 EmpowHER-BC-303 breast cancer trial now enrolling
- Initiated Phase 2 DiscovHER-Pan-206

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

- **ZW171 (Phase 1 Initiated)**
MSLN x CD3 bispecific antibody
- **ZW191 (Phase 1 Initiated)**
FR α TOPO1i ADC
- **ZW220 (IND 1H 2025)**
NaPi2b TOPO1i ADC
- **ZW251 (IND 2H 2025)**
GPC3 TOPO1i ADC
- **Candidate 5 TBD (IND 1H 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 US approval and launch of zanidatamab. Cash runway forecast into 2H 2027, with receipt of certain anticipated regulatory milestone payments.

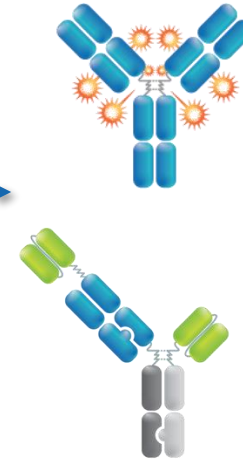
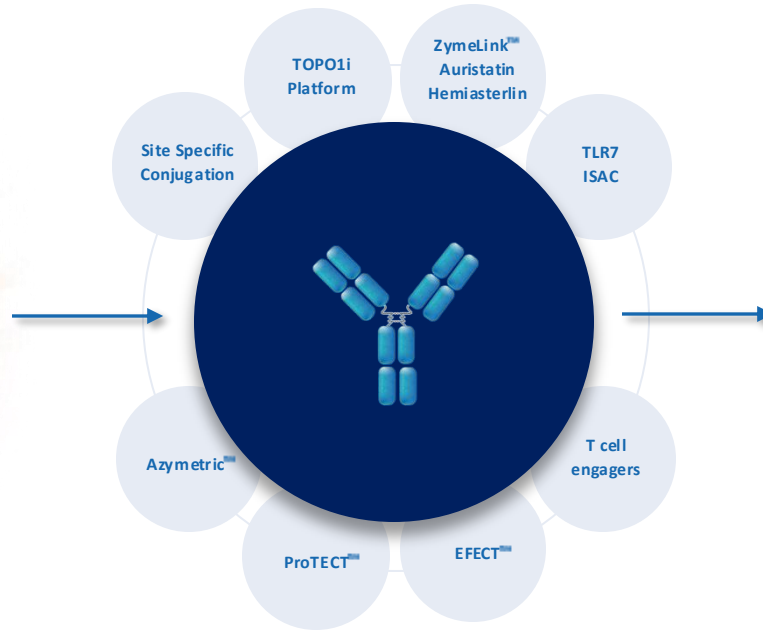
1L: first-line (treatment); 2L: second-line (treatment); ADC: antibody-drug conjugate; BLA: Biologics License Application; BTC: biliary tract cancers; CD3: cluster of differentiation 3 protein complex and T cell co-receptor; FR α : folate receptor alpha; FDA: U.S. Food and Drug Administration; GEA: gastroesophageal 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; PDUFA: Prescription Drug User Fee Act; 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 novel therapeutics expected to be in active clinical trials by 2026

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

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

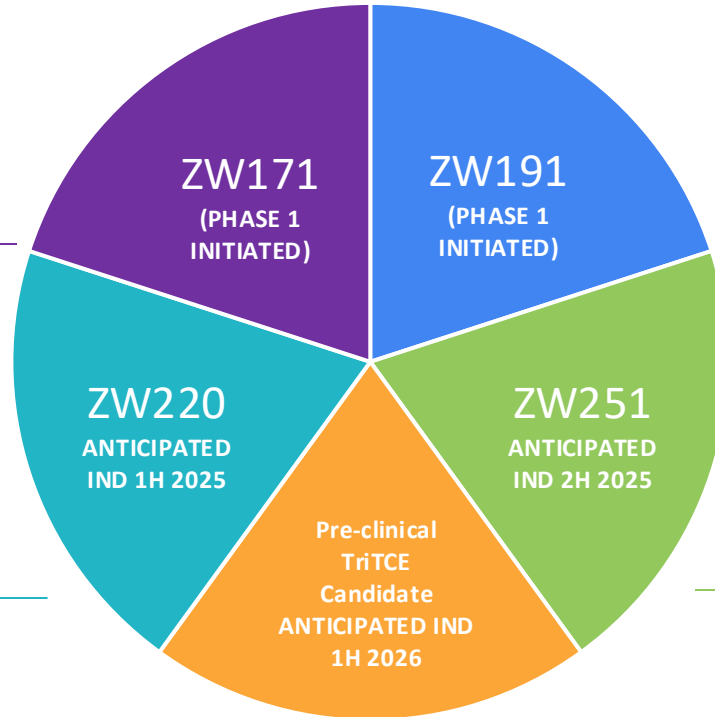


ZW171 (MSLN)

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 (FR α)

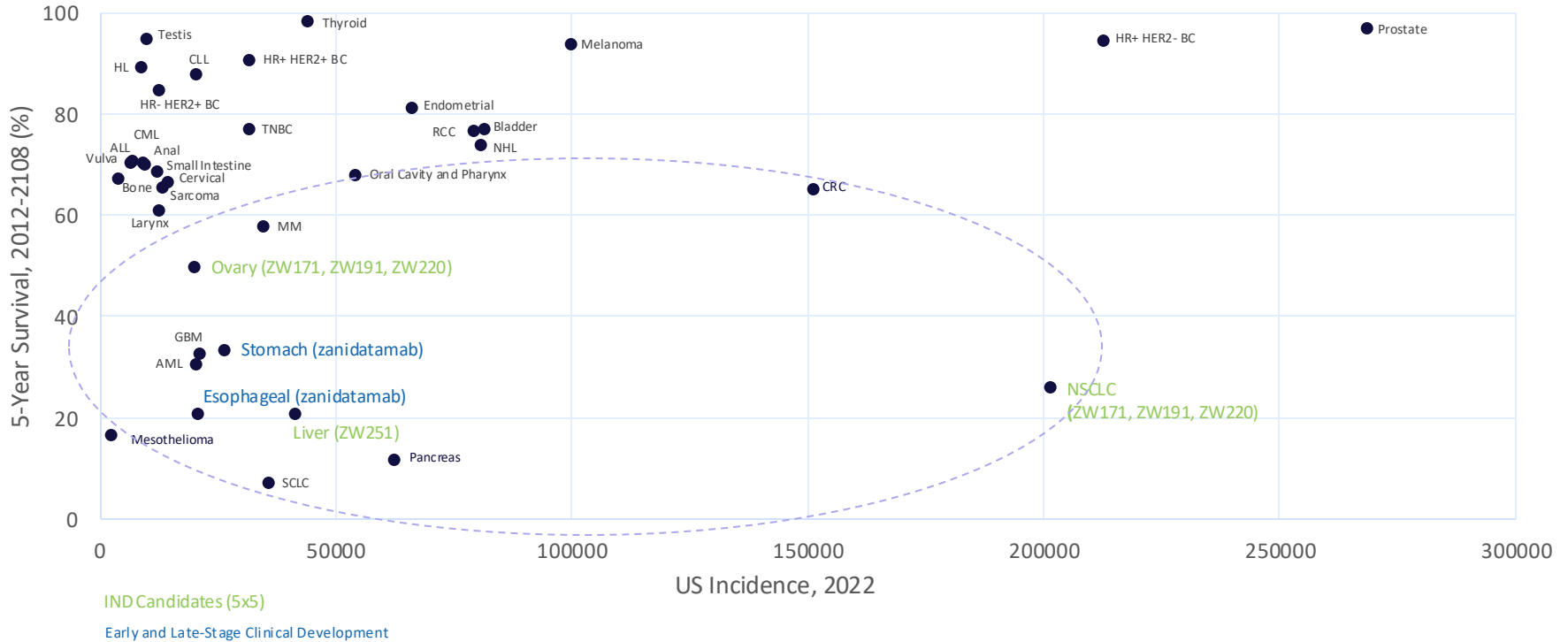
Antibody-Drug Conjugate targeting folate receptor alpha expressing tumors including ovarian, other gynecological, and non-small cell lung cancer

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 News Flow Completed in 2024 and Expected in 2025

1H 2024

2H 2024

2025

PIPELINE EVENTS

- BLA accepted and granted Priority Review in the USA by our partner Jazz for zanidatamab in 2L BTC
- Jazz initiated a Phase 3 global confirmatory trial for zanidatamab in 1L BTC
- Jazz Initiated Phase 3 EmpowHER trial in late-line HER2+ breast cancer.
- Jazz confirmed that the European Medicines Agency validated the Marketing Authorization Application for zanidatamab in 2L BTC

- BLA accepted in China by our partner BeiGene for zanidatamab in 2L BTC
- Phase 1 Initiated for both ZW171 & ZW191
- Jazz initiated a Phase 3 trial for zanidatamab in patients who have progressed on previous T-DXd treatment by our partners Jazz
- Nomination of Tri-TCE product candidate
- U.S. FDA approval and launch of Ziihera® (zanidatamab-hii) for the treatment of adults with previously treated, unresectable or metastatic HER2+ (IHC 3+) BTC 2L
- Jazz Initiated Phase 2 DiscovHER-Pan-206
- [Virtual & In-Person R&D Day](#) in New York on December 12, 2024

- Pivotal Phase 3 top-line data readout in GEA 1L targeted by our partner Jazz in 2Q 2025
- Potential China approval for zanidatamab in 2L BTC in Q2 2025
- Initial royalty revenue from partners Jazz and BeiGene
- Expected IND submission for ZW220 (NaPi2b) in 1H 2025
- Expected IND submission for ZW251 (GPC3) in 2H 2025

PUBLICATIONS & CONFERENCES

- ASCO GI (January 18-20)
- JSMO (February 22-24)
- World ADC London (March 12-15)
- AACR (April 5-10)
- PEGS (May 13-17)
- ASCO (May 31-June 4)

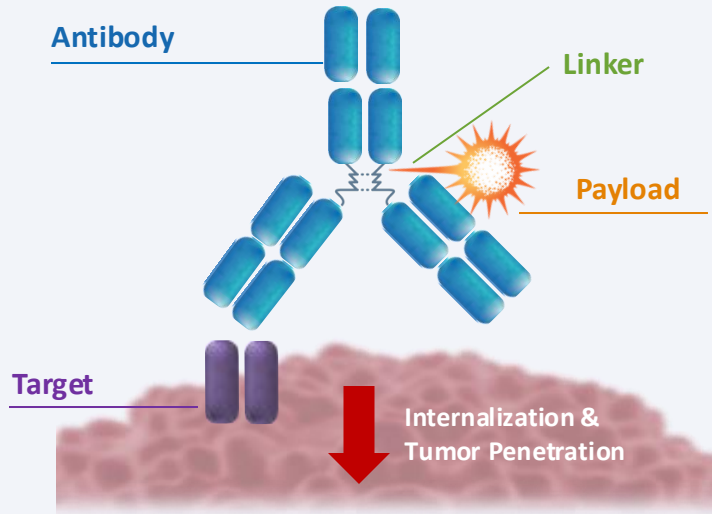
- WCGQ (July 3-6)
- ESMO (September 13-17)
- EORTC-NCI-AAACR (October 23-25)
- SITC (November 6-10)
- SABCS (December 10-14)

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-AAACR: EORTC-NCI-AAACR 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.

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.



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>

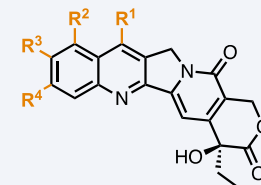
Despite a prevailing dogma wherein antibody drug conjugates (ADCs) increase the maximum tolerated dose of potent cytotoxic payloads while lowering the minimum effective dose, mounting clinical evidence argues that the tolerated doses of ADCs are not significantly different from those of related small 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

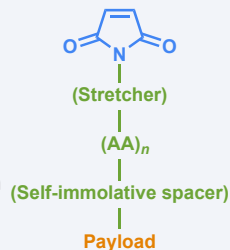
- Acknowledges complex mechanisms driving TOPO1i ADC action
- Sufficient tolerability to achieve ADC dose > 5 mg/kg



Linker

Traceless, plasma-stable, cleavable peptide

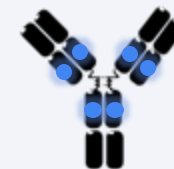
- Common to majority of approved ADCs
- Compatible with desired bystander activity
- Avoids highly stabilized linker-antibody conjugation to limit off target toxicities



Conjugation

Thiol-maleimide chemistry

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



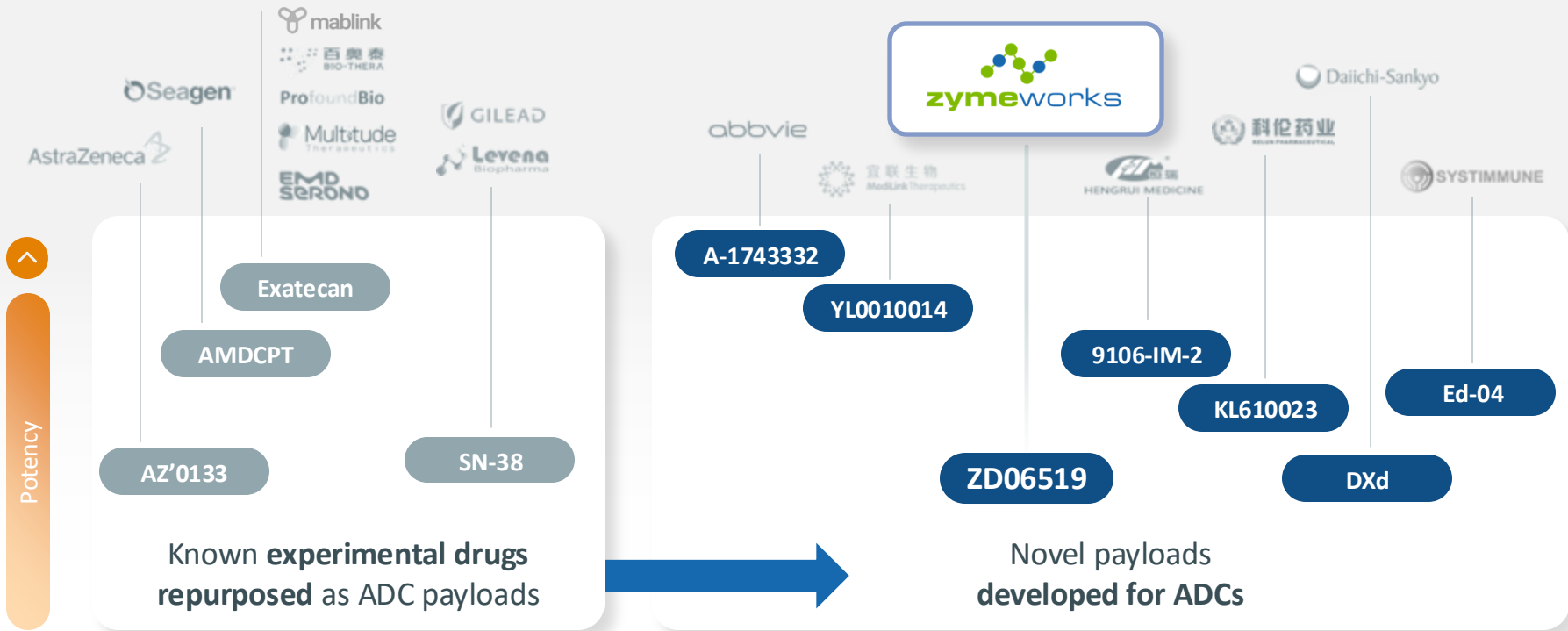
Differentiated Development of Antibody-Drug Conjugates

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 ADC targeting folate receptor-alpha	OVCA, other gynecological cancers, NSCLC	FR α	Topoisomerase I Inhibitor (ZD06519)	8		NC T06555744		Phase 1 clinical trial initiated	
ZW220 ADC targeting Napi2b	OVCA, NSCLC	NaPi2b	Topoisomerase I Inhibitor (ZD06519)	4				On track for IND filing in 1H 2025	
ZW251 ADC targeting GPC3	Hepatocellular carcinoma	GPC3	Topoisomerase I Inhibitor (ZD06519)	4				On track for IND filing in 2H 2025	

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 FR α -targeting ADC

FR α is found in ~75% of high-grade serous ovarian carcinomas¹ and ~70% of lung adenocarcinomas²



Optimized Design³

- 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 FR α expression³
- Favorable safety profile in non-human primate toxicology studies³
- Opportunity to treat broader range of FR α -expressing cancers



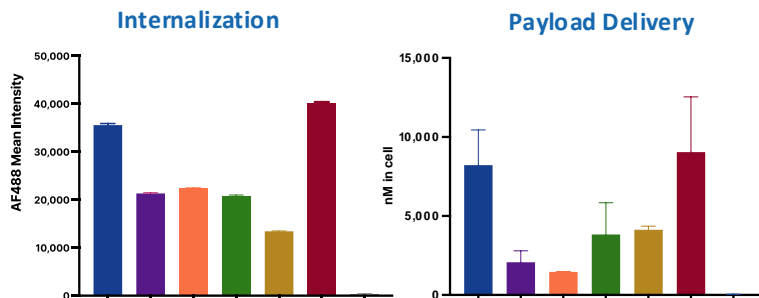
Status

- Initiated Phase 1 clinical trial (NCT06555744)

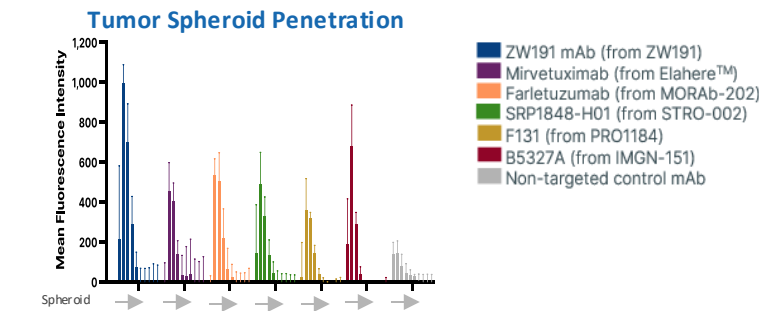
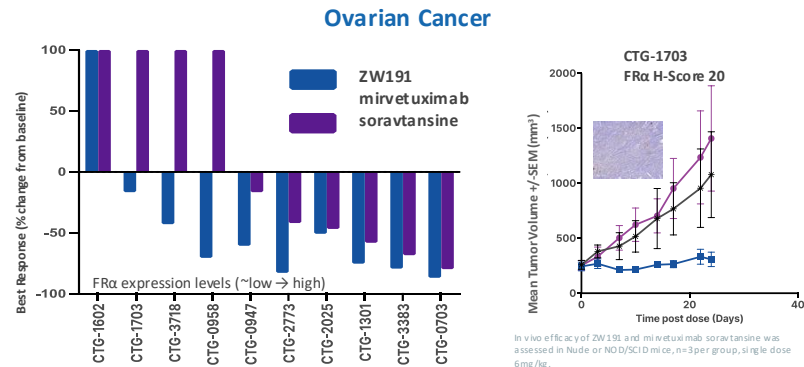
1. Köbel, M., Madore, J., Ramus, S. et al. Br J Cancer 111, 2297–2307 (2014).
 2. O'Shannessy DJ, et al., Oncotarget. 2012 Apr; 3(4):414-25.
 3. Lawn S et al. Abstract #2641 Presented at AACR 2023.

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

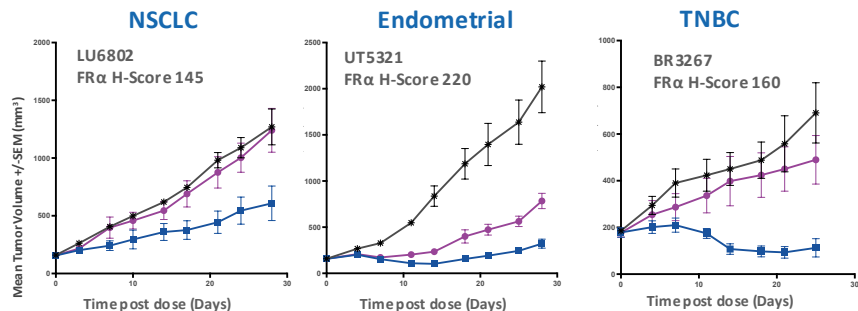
ZW191's Novel mAb Drives Superior Internalization, Payload Delivery, and Tissue Penetration



Anti-tumor Activity Across Multiple Tumor Types And Range of FR α Expression (PDX models)



In vitro functional assessment of the antibody properties of ZW191 and other FR α -targeted ADCs and a non-targeted control mAb (all WT Fc to facilitate comparison). Internalization of AF488 labeled antibodies to KB-Hela cells after 24 hrs at 300 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 FR α -targeted mAb conjugated to ZymeLink™ Auristatin (ZLA); Penetration of AF488 labeled antibodies as quantified by high content imaging of spheroid layers at 24 hours post-treatment at 50 nM.



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

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; Lawin S. et al. Abstract# 1862 presented at American Association for Cancer Research annual meeting 2024.

ZW191: Novel and Proprietary TOPO1i Payload Well-Tolerated

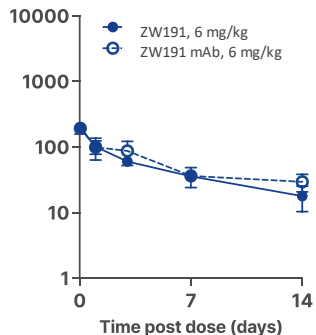
ZW191 shows a favorable tolerability profile of 60 mg/kg in NHP¹

Dose mg/kg	Observations	Histopathology	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			

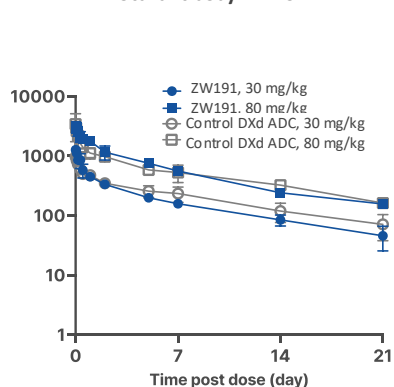
- No mortality or body weight effects
- No ophthalmic effects
- All effects were non-adverse and reversible
- HNSTD in NHP of 60 mg/kg presents a compelling profile, enabling expectation of achieving efficacious dose level

ZW191 has a favorable pharmacokinetic (PK) profile²

Total Antibody PK from a Mouse Xenograft study



Total antibody PK from NHP



- **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 primate; PACS: pancreatic acinar cell secretion.

1. Law S. et al. ZW191 – a FRA-targeting antibody-drug conjugate with strong preclinical activity across multiple FRA-expressing indications. Abstract # 1862 presented at American Association for Cancer Research annual meeting 2024.

2. Law 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 FR α ADC Space for TOPO1i

A novel design to target FR α

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.

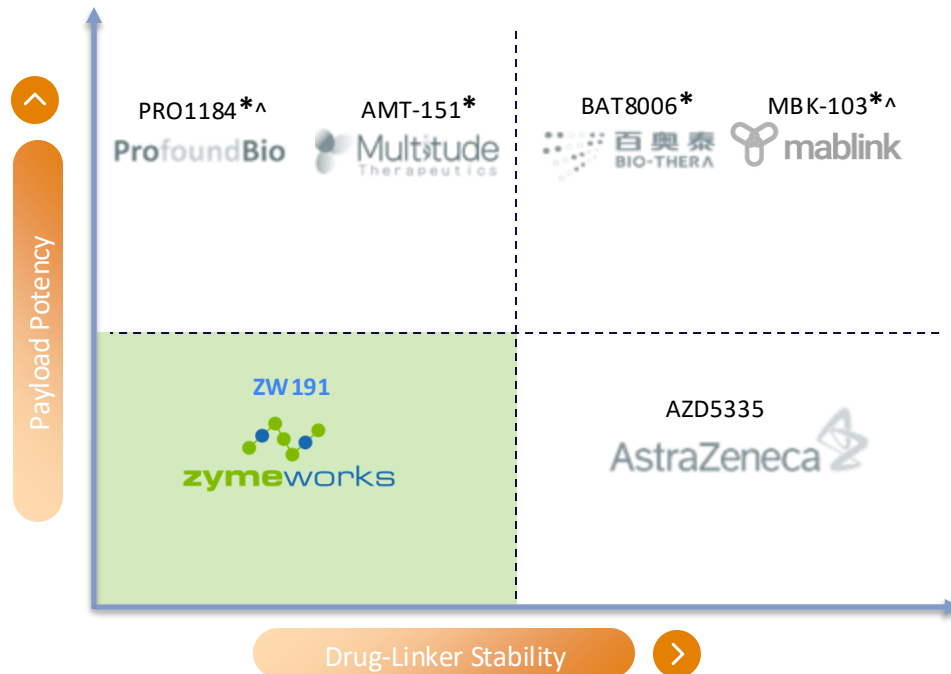
4. Moderate antibody-linker stability

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 FR α .¹

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



1. Law 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. Clin. Oncol. 2023 09:1924; 4. Colombo R, Barnsder SD, Rich J R. Cancer Res 2023, 83 (7). Abstract #1538 presented at AACR 2023 5. Law S. ZW191: A Potential Best-in-Class TOPO1i ADC for Treatment of FR α -Expressing Solid Tumors, Presented at World ADC London 2023.

* Denotes use of exatecan payload

^ Denotes use of Fc-silenced antibody

ZW191 Global Phase 1 Study in FR α -Expressing Solid Tumors (NCT06555744)

Open-label, FIH, dose-escalation study N= ~145

Part 1: Dose Escalation

Advanced ovarian, endometrial, NSCLC malignancies
FR α IHC +/-

MTD/RD determined

Part 2a: Dose Optimization

Ovarian cancer^a

Cohort 1: Ovarian^a

Ovarian cancer participants randomized into 2 dose levels as follows:

- Dose Level A
- Dose Level B

Part 2: Dose Expansion

Part 2b: Dose Expansion

Endometrial cancer and nonsquamous NSCLC

Cohort 2: Endometrial

Endometrial cancer participants
FR α positive. Dose level TBD^b

Cohort 3: Nonsquamous NSCLC

Nonsquamous NSCLC participants
FR α positive. Dose level TBD^b



Treatment until disease progression, unacceptable toxicity, or withdrawal of consent

Part 1: Dose Escalation

Primary Endpoint

- Safety and tolerability
- MTD/MAD

Secondary Endpoints

- PK, ADA
- cORR (RECIST)

Part 2: Dose Expansion

Primary Endpoints

- OBD
- Safety and tolerability
- cORR

Secondary Endpoints

- PK, ADA
- PFS
- DOR
- OS

KEY ELIGIBILITY CRITERIA

Inclusion criteria

- Pathologically confirmed ovarian cancer, endometrial cancer, NSCLC
- Progressive disease refractory to all SOC^cs that confer clinical benefit
- Measurable disease per RECIST v1.1
- ECOG PS 0-1
- Adequate organ function

Exclusion criteria

- Known additional malignancy that is progressing or that has required active treatment
- Ongoing clinically significant toxicity (Grade ≥ 2)
- Advanced/metastatic, symptomatic, visceral spread, at risk of life-threatening complications in the short-term

^aOvarian cancer includes primary peritoneal and fallopian tube cancers. ^bPart 2 will be initiated at dose levels (RDEs) based on the SMC's comprehensive analysis of safety, tolerability, clinical PK, PD, and preliminary antitumor activity data from Part 1. The Part 2 selected doses will be decided at SMC meetings and could be the MTD or RDEs based on comprehensive analysis of safety, tolerability, clinical PK, PD, and antitumor activity data from Part 1. The RDE dose levels may vary across the tumor types in Cohorts 1, 2, and 3. ^cTimed from cycle 1 day 1. Q6W (every 6 weeks) for the first 4 assessments and then Q9W (every 9 weeks) thereafter. ClinicalTrials.gov ID: NCT06555744.

ADA: anti-drug antibody; ADC: antibody-drug conjugate; AE: adverse event; AESI: adverse event of special interest; CNS: central nervous system; CT/MRI: computed tomography/magnetic resonance imaging; ECOG PS: Eastern Cooperative Oncology Group performance status; FR α : folate receptor alpha; IHC: immunohistochemistry; IV: intravenous; MTD: maximum tolerated dose; NSCLC: non-small cell lung cancer; ORR: objective response rate; PD: pharmacodynamics; PK: pharmacokinetics; Q3W: every 3 weeks; RDE: recommended dose for expansion; RECIST: Response Evaluation Criteria in Solid Tumors; SAE: serious adverse event; SMC: safety monitoring committee; SOC: standard of care; TBD: to be determined; TOPO1i: topoisomerase-1 inhibitor.



ZW220

NaPi2b-targeting ADC

NaPi2b is found in ~96% of ovarian serous adenocarcinomas¹ and ~87% of non-small cell lung adenocarcinomas¹



Design²

- 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 expression¹
- Encouraging tolerability in repeat dose non-human primate toxicology studies²
- First-in-class ADC potential for NaPi2b-expressing solid tumors



Status

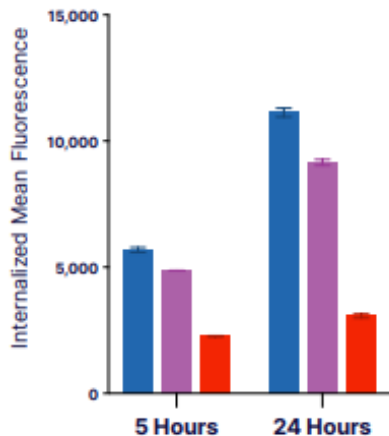
- Expected IND filing in 1H 2025

1. Lin K, et al. *Cl in 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.

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

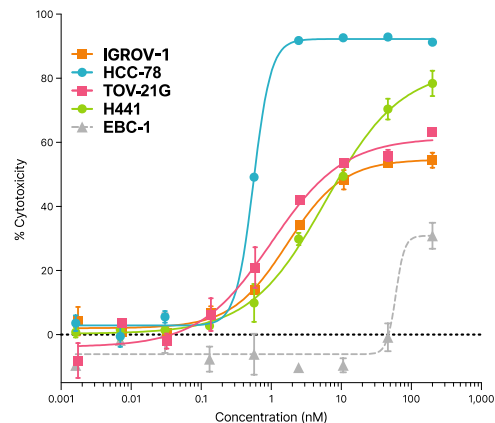
Efficient and Rapid Internalization



■ ZW220 mAb
 ■ tamab
 ■ Lifas mab

Growth Inhibition in Ovarian Cancer and NSCLC Models

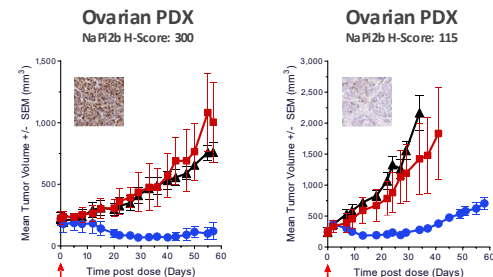
ZW220 DAR 4 cytotoxicity in 3D spheroids



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

Anti-Tumor Activity in Ovarian Cancer Models

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



▲ Vehicle
● ZW220 (6 mg/kg)
■ lifastuzumab vedotin (6 mg/kg)

Cell line spheroids with NaPi2b/Cell expressed: IGROV-1 (Ovarian) 1,770,000 expressed; HCC-78 (NSCLC) 820,000 expressed; TOV-21G (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.

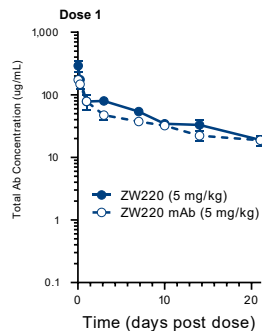
ZW220: Novel and Proprietary TOPO1i Payload Well-Tolerated

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	

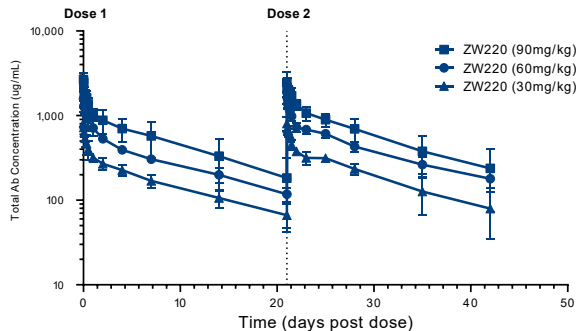
- The MTD of ZW220 in NHPs is 90 mg/kg
- No mortality or adverse pathology findings were observed at high doses

ZW220 has a favorable pharmacokinetic (PK) profile

Total Antibody PK from a Tg32 Humanized FcRn Mice



Total antibody PK from NHP

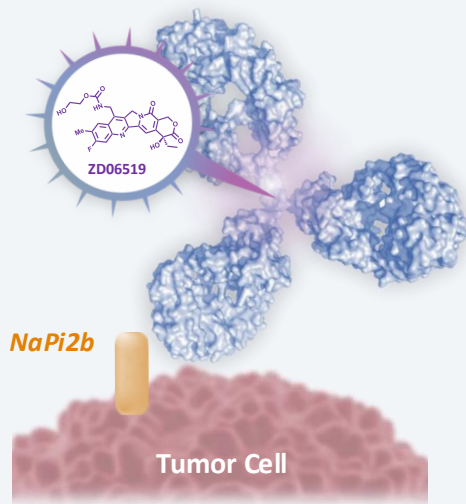


- **ZW220** displays desirable PK characteristics and is well tolerated at high doses
- IND enabling activities are underway

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

ZW220: A NaPi2b-Targeting Antibody-Drug Conjugate

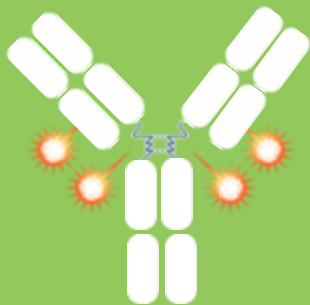
Design



	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 ^{1,2,3}
2	Topoisomerase I inhibitor (TOPO1i) payload mechanism	Proven ADC mechanism in solid tumors across multiple tumor-associated antigens ¹
3	Moderate payload potency	NHP MTD ≥ 90 mg/kg; potential for high doses in humans
4	Moderate antibody-linker stability	Limits antibody-driven toxicities ⁴
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 ^{1,5}
7	FcγR silenced	Potential to minimize toxicities driven by cellular uptake via FcγR ^{6,7,8}

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

1. Hernandez Rojas A et al. Presentation at World ADC 2023; 2. Hernandez Rojas A et al. Abstract# 1533 presented at AACR 2023; 3. Zhang D, et al. Drug Metab Dispos. 2019;47(10):1146-1155; 4. Colombo R. Presentation at AACR-NCI-EORTC 2023; 5. Okajima D, et al. Mol Cancer Ther. 2021;20(12):2329-2340; 6. Mahalingaiah PK, Pharmacol Ther. 2019;200:110-125; 7. Kumagai K, et al. Cancer Sci 2020; 111: 4636-4645; 8. Koganemaru S, et al. Abstract#5760 presented at AACR 2024.



ZW251

Glypican 3-targeting ADC

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



Design²

- 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 expression²
- Noteworthy tolerability in repeat dose non-human primate toxicology studies²
- First-in-class ADC potential for HCC
- Glypican 3 is expressed in 76% of hepatocellular carcinomas (HCC), with high expression observed in ~55% of HCC¹



Status

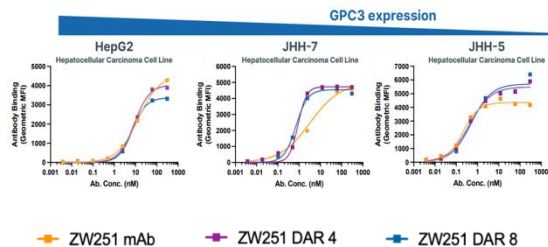
- Expected IND in 2H 2025

ZW251: Potential Utility in Hepatocellular Carcinoma^{1,2}; On Track for Clinical Studies in 2025

ZW251 demonstrates target-mediated uptake and anti-tumor activity

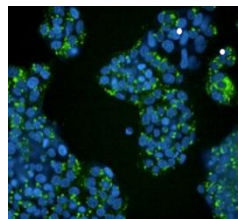
Selected For Strong Binding Over Various Levels Of Expression

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



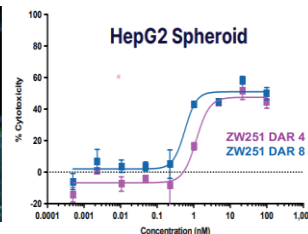
Enhanced ADC Internalization and Cytotoxicity

ZW251 internalized in HepG2 cell line



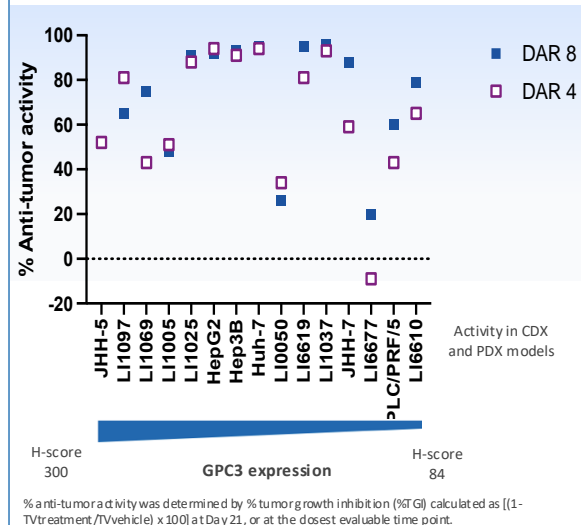
Internalization visualized after 24-hour treatment

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

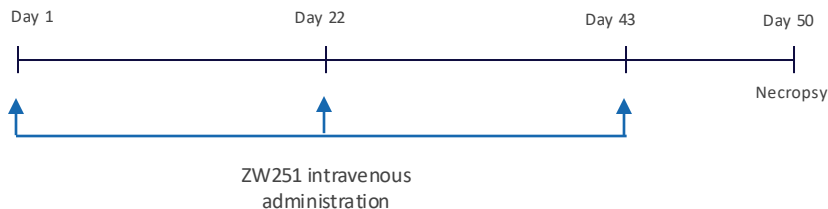


CDX: cell derived xenograft.

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

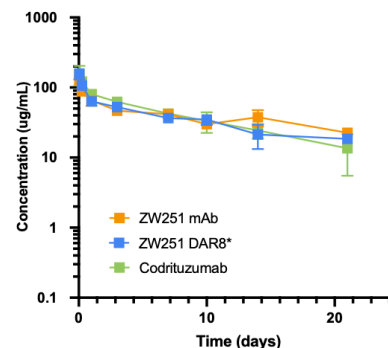
Three Dose Non-Human Primate (NHP) Toxicology Study



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)

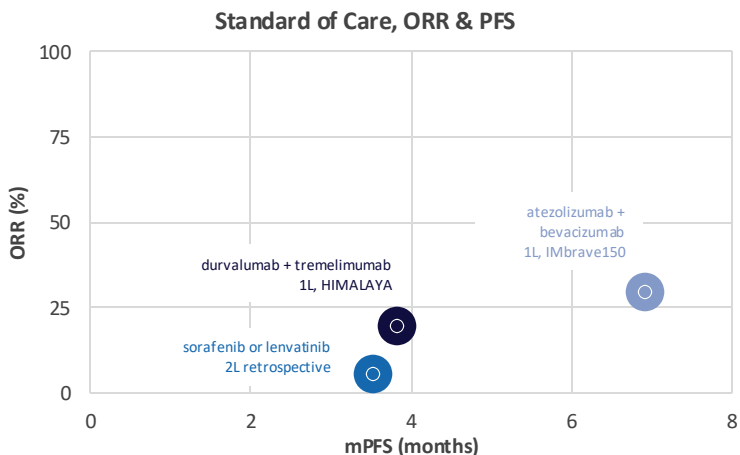
mAb: monoclonal antibody; PK: pharmacokinetics.

Madera L et al., ZW251, a novel glypica n-3-targeting antibody-drug conjugate bearing a topoisomerase I inhibitor payload. Abstract# 2658 presented at AACR 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 cancer¹
- 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/>.

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	U.S. FDA Approval in 2L BTC, 1L confirmatory study underway				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)	NCT06523803		Phase 1 clinical trial initiated		
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™				

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*



1

Entering market first in BTC with U.S. FDA Approval¹

- U.S. FDA approval and launch of Ziihera® (zanidatamab-hrii) for the treatment of adults with previously treated, unresectable or metastatic HER2+ (IHC 3+) BTC 2L
- The CDE NMPA in China has accepted the BLA for zanidatamab for 2L BTC
- Confirmatory Phase 3 trial initiated in 1L metastatic BTC



Represents ~12,000 HER2+ cases annually² in USA, Europe³, 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 choice¹
- Opportunity to explore potential in neoadjuvant populations¹



Represents larger patient opportunity with ~63,000 HER2+ cases annually² in USA, Europe³, and Japan

3

Expanded opportunity across lines of Breast Cancer (BC)¹

- Early lines of therapy (neoadjuvant)
 - Post T-DXd
 - Novel combinations¹
- Ongoing trials in early breast cancer:
- I-SPY2 Trial⁴
 - MD Anderson collaboration
 - Phase 3 EmpowHER-BC-303 trial



Considerable market opportunity with more than 150,000 cases annually⁵ in USA, Europe³, and Japan

4

Broad potential beyond BTC, GEA, and mBC in multiple HER2-expressing indications⁶

- Initiated Phase 2 DiscoverHER-Pan²⁰⁶
- Colorectal
 - NSCLC
 - Ovarian
 - Endometrial
 - Pancreatic
 - Bladder
 - Salivary Gland
 - Ampullary
 - And other HER2-expressing solid tumors

*Adapted from Jazz Pharmaceuticals' Guidance

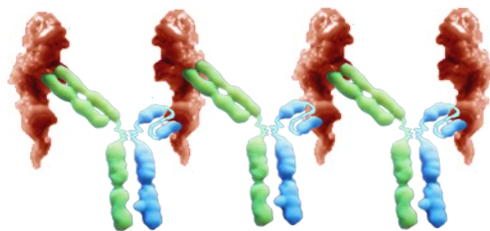
sBLA: supplemental biologics license application; CDE: Center for Drug Evaluation; NMPA: National Medical Products Administration.

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](https://doi.org/10.1016/S1470-2045(22)00621-0).

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 downregulation¹
- Inhibition of cellular proliferation
- Fc-mediated cytotoxicity: ADCC, ADCP, CDC¹
- FDA Breakthrough Designation

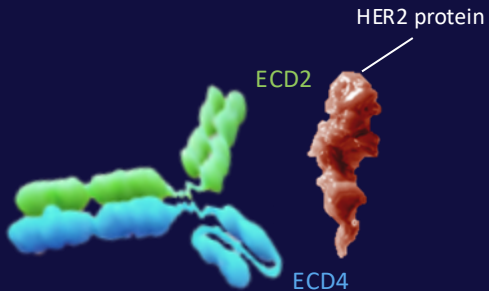
Biparatomic HER2-Binding of Zanidatamab Drives Multiple Mechanisms of Action



The geometry of zanidatamab prevents it from binding to the same HER2 molecule¹

Zanidatamab

A Bispecific Antibody for
HER2-Expressing Cancers



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)¹, 14.9 months mDoR²

Combination Activity in First-Line GEA studies

- 79% ORR with a mDOR of 20.4 months and 84% 18-month OS rate³
- 75.8% ORR with mDOR 22.8 months and mPFS 16.7 months⁴

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 Oncology¹ & longer follow-up including overall survival findings at ASCO 2024²

HERIZON-GEA-01

A Global Pivotal Study in First-Line HER2-Positive GEA⁵

- Supported by promising Phase 2 clinical data presented at ASCO GI 2023³ and Phase 1b/2 data at ESMO 2023⁴



Key Milestones

- U.S. FDA approval and launch of Ziihera® (zanidatamab-hrii) for the treatment of adults with previously treated, unresectable or metastatic HER2+ (IHC 3+) BTC 2L
- The CDE NMPA in China has accepted the BLA for zanidatamab for 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 2Q 2025

Collaboration Partners:




mDOR: median duration of response; OS: overall survival; mPFS: median progression-free survival

1. Harding et al., Lancet Onco 2023; 2. Pant et al., Abstract #4091 presented at ASCO 2024; 3. Elmova E et al., Abstract #347 presented at ASCO GI 2023, JCO 41(45); 4. Lee KW et al., Abstract # 3088 presented at ESMO 2023; 5. NCT05152147.

Zanidatamab: Licensing Agreement with Jazz



Licensing Agreement Terms ¹	
Counterparty	 Jazz Pharmaceuticals
Upfront Payments	\$375M received in 4Q22
BTC Milestone Payment	Zymeworks is eligible to receive \$25M
Remaining Regulatory Milestones	Up to \$500M
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) 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 Terms¹

Counterparty	
Upfront Payments	\$40M
Development and Commercial Milestones	Up to \$164M remaining
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

- Zymeworks has received \$53 million in upfront and milestone payments as well as certain co-development funding for zanidatamab clinical studies, not including the \$8 million milestone payment in connection with the CDE NMPA's acceptance of the BLA for zanidatamab for 2L BTC
- We remain eligible to receive up to \$164 million in additional development and commercial milestones from the original \$195 million
- 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 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 ICR¹)

Secondary End Points: Proportion of patients with DOR \geq 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 Oncology².

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 chemotherapy³, 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 BICR¹)

Secondary End Points: ORR, DOR, Safety, HRQoL

Additional Details: Anticipate topline readout in 2Q 2025

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).

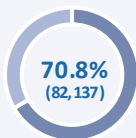
Zanidatamab: Epidemiology of Biliary Tract Cancers

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



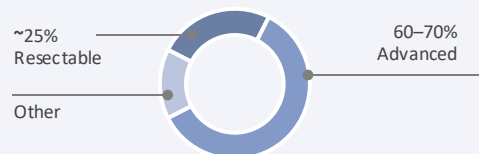
of all estimated new GBC cases occurred in Asia, with 10% (~12,570) in Europe in 2020⁷

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 States⁸ 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 months¹⁴ with a recent phase II trial reporting 8.6 months¹⁵
- ~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
HER2¹⁷

1. Bogenberger JM et al., Precision Oncol. 2018; 2. Laczcano-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 include 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 NJ et al., Biomolecules. 2021; 13. Fomaro 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 options²

Guideline option from the ABC-02 trial³

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 trial⁶

cisplatin + gemcitabine + pembrolizumab

ORR = 28.7%_{BICR}, mPFS = 6.5 months,
mOS = 12.7 months

Progression in Metastatic Biliary Tract Cancers

Second-line treatment options²

Guideline option from the ABC-06 trial⁷

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 months⁸

IDH1 mutation: mPFS = 2.7 months, mOS = 10.3 months⁹

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

trastuzumab + FOLFOX mPFS = 5.1 months, mOS = 10.7 months¹⁰

TDXd (HERB trial) mPFS = 5.1 months, mOS = 7.1 months¹¹

trastuzumab + pertuzumab (MyPathway) mPFS = 4.0, mOS = 10.9 months¹²

BRAF: activating serine/threonine-protein kinase B-raf kinase; ERBB2: receptor tyrosine-protein kinase erbB-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 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. Fin R et al., ASCO 2024 7. Lamarca et al., J Clin Oncol 2019; 8. Vogel A et al., Ann 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 2024; 12. Sweeney et al., J Clin Oncol 2023.

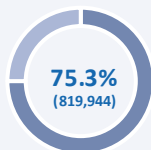
Zanidatamab: Epidemiology of Gastroesophageal Adenocarcinoma

- 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 regions⁴
- 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

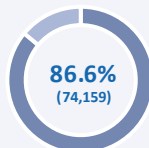
Incidence rates¹¹

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 rates¹¹

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. Sitaz 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 Cutsem 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 trial⁴

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 trial⁵
(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 = 20.1 vs 15.7months

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}

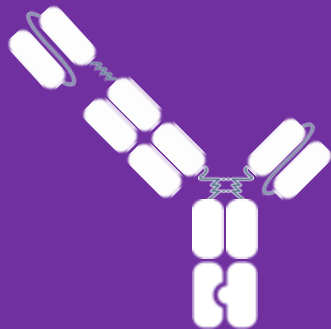
CPS: combined positive score; GEJ: gastroesophageal junction; HER2+: epidermal growth factor receptor 2 positive; ITT: intention-to-treat population; mOS: median overall survival.

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 al., Lancet 2010- TOGA updated OS (13.1 vs 11.7months) reported in FDA label, accessed https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/103792s250lbl.pdf; 5. Janjigian Y et al., ESMO 2024.

Zanidatamab: Regulatory Designations, Exclusivity & IP

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



Design¹

- 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



Profile¹

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



Status

- Initiated Phase 1 clinical trial (NCT06523803)

scFV: single-chain variable fragment.

1. Afacan N et al., Abstract #2942 presented at AACR 2023.

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

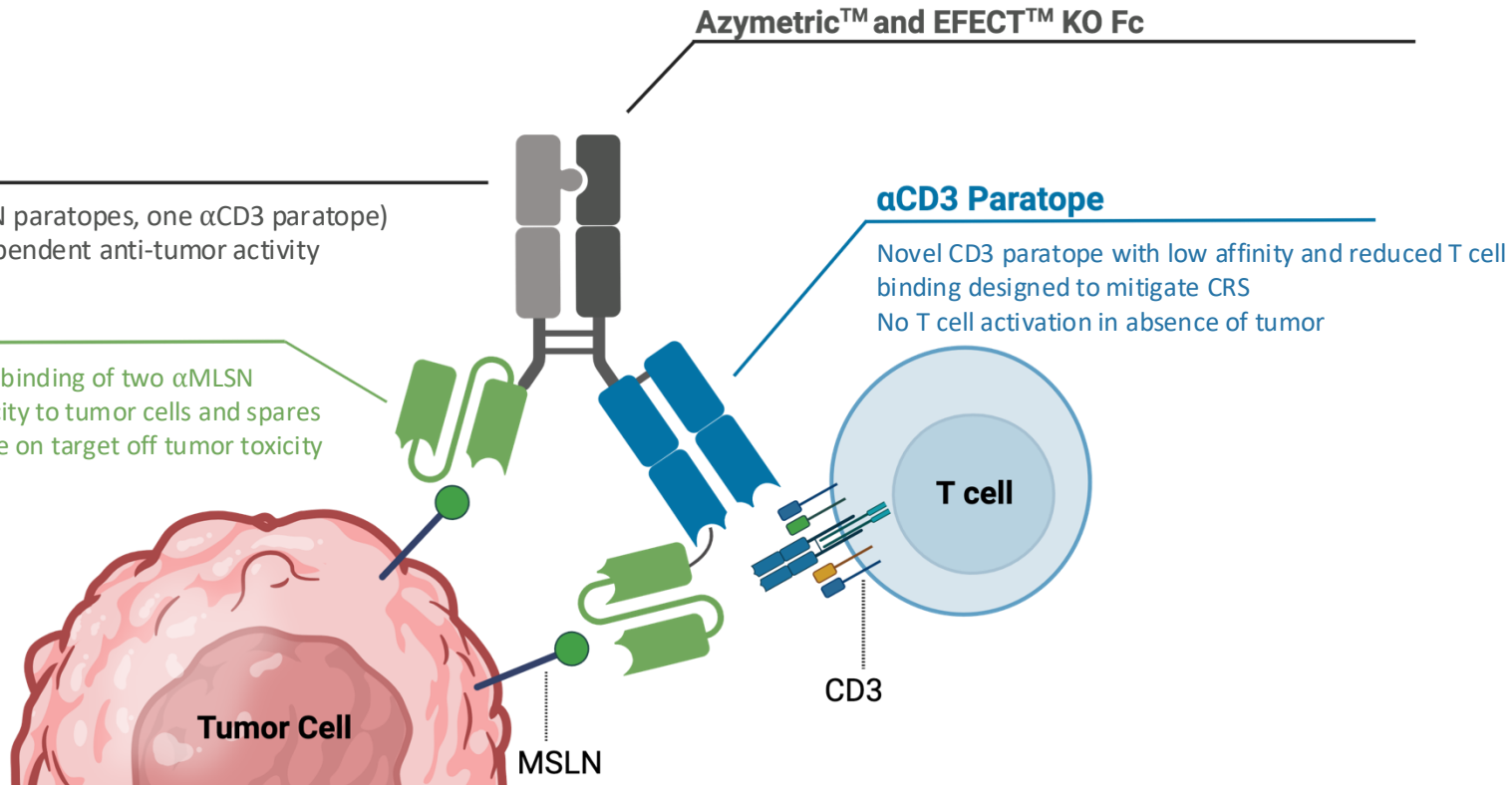
ZW171: Designed to Widen the Therapeutic Window with Enhanced Safety and Anti-Tumor Activity

Antibody Format

2 +1 format (two α MSLN paratopes, one α CD3 paratope) optimized for tumor-dependent anti-tumor activity

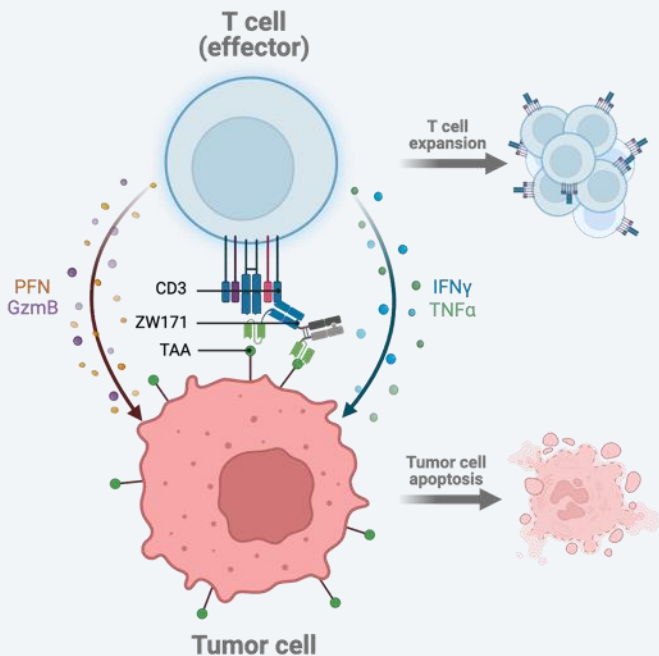
α MSLN Paratopes

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



CRS: cytokine release syndrome.

ZW171: A MSLN-Targeting T Cell Engaging Bispecific Antibody



Design Feature

Expected Benefit

1 Optimized 2 + 1 Format

- Avidity-driven binding drives cytotoxicity to tumor cells and spares normal tissues to mitigate on target off tumor toxicity
- 2+1 format (two α MSLN paratopes, one α CD3 paratope) optimized for enhanced antitumor activity

2 Novel α CD3 paratope with low affinity

- Reduced T cell binding to mitigate CRS
- No T cell activation in absence of tumor
- Supports effective target-dependent tumor cell killing
- Anti-MSLN scFv paratope proximity to anti-CD3 Fab functions to further reduce T cell binding

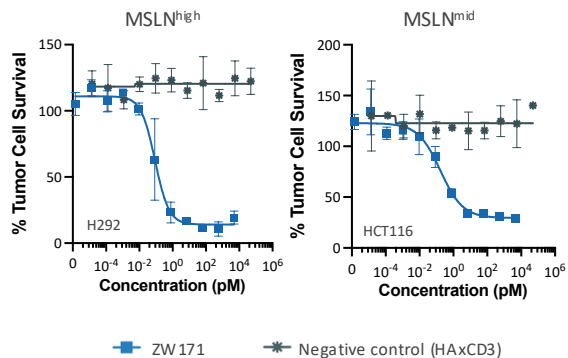
3 Fc γ R silenced with EFECTTM

- Avoid T cell activation mediated by Fc γ R engagement

ZW171: Key Design Considerations

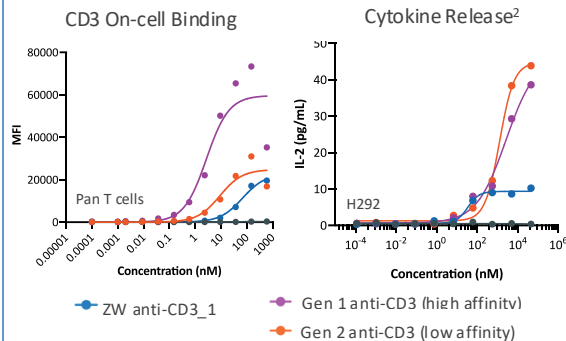
Engineered with 2+1 Format Facilitates Avidity-Driven Binding¹

Tumor Cell Cytotoxicity in Mid-to-High Expressing MSLN Models¹



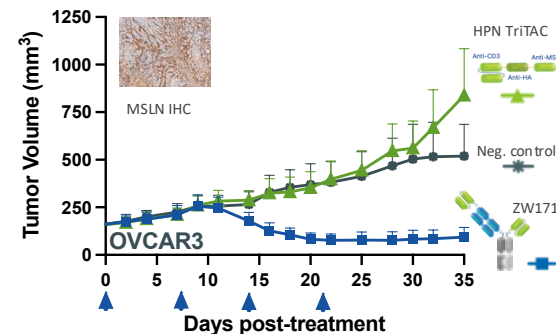
Novel CD3 Paratope with Enhanced Safety

Proprietary CD3 engager has low affinity CD3 binding and cytokine release¹



Pilot NHP toxicology data shows ZW171 is well-tolerated up to 30 mg/kg¹

Differentiated by Greater Anti-Tumor Activity in MSLN-Expressing Tumor Models¹



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.

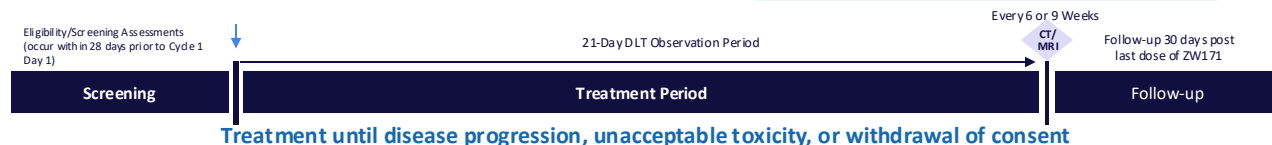
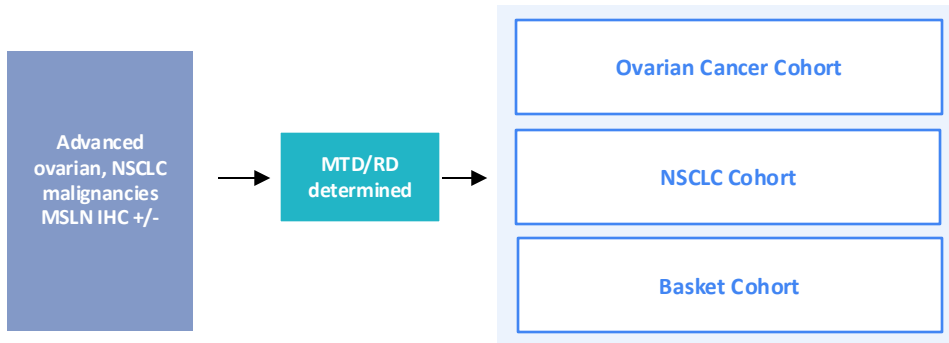
Global Phase 1 Study in MSLN-Expressing Solid Tumors (NCT06523803)

Open-label, FIH, dose-escalation study

Part 1: Dose Escalation

N= ~160

Part 2: Dose Expansion



Part 1: Dose Escalation		Part 2: Dose Expansion	
Primary Endpoint <ul style="list-style-type: none"> Safety and tolerability MTD/MAD 	Secondary Endpoints <ul style="list-style-type: none"> PK, ADA cORR (RECIST) 	Primary Endpoints <ul style="list-style-type: none"> OBD Safety and tolerability cORR 	Secondary Endpoints <ul style="list-style-type: none"> PK, ADA PFS DOR OS

KEY ELIGIBILITY CRITERIA

Inclusion criteria

- Pathologically confirmed of cancers with evidence of locally advanced (unresectable) and/or metastatic disease. Cancers that are refractory to all available SOC treatment, cancers for which no SOC treatment is available, or the participant cannot tolerate or refuses SOC therapy
- ECOG PS 0 or 1
- Adequate organ function

Exclusion criteria

- Known additional malignancy that is progressing or that has required active treatment
- Ongoing clinically significant toxicity (Grade ≥ 2)
- Advanced/metastatic, symptomatic, visceral spread, at risk of life-threatening complications in the short-term

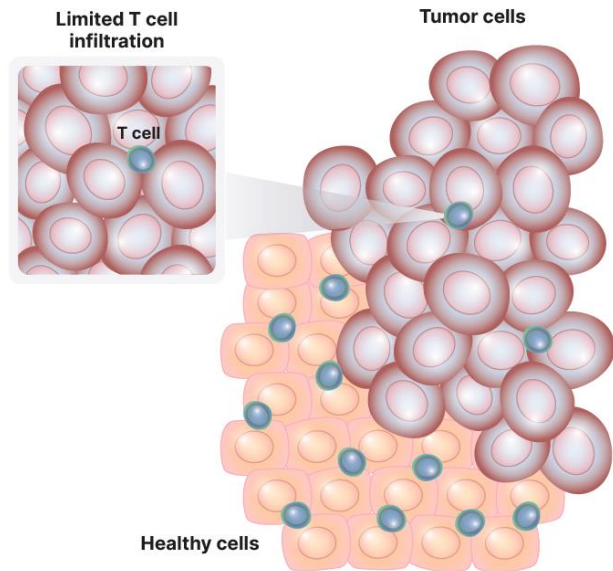
ADA: anti-drug antibodies; cORR: confirmed objective response rate; DL: dose level; DOR: duration of response; ECOG: Eastern Cooperative Oncology Group; FIH: first in human; GEA: gastrointestinal adenocarcinomas; IHC: immunohistochemistry; MAD: maximum administered dose; MTD: maximum tolerated dose; MSLN: mesothelin; mTP: modified toxicity probability interval; NSCLC: non-small cell lung cancer; OBD: optimal biological dose; OS: overall survival; PFS: progression-free survival; PK: pharmacokinetics; pts: patients; PS: preferred status; Q3W: every 3 weeks; RD: recommended dose; SC: subcutaneous; SOC: standard of care; TBC: to be confirmed

Multispecific Antibody Therapeutic Development

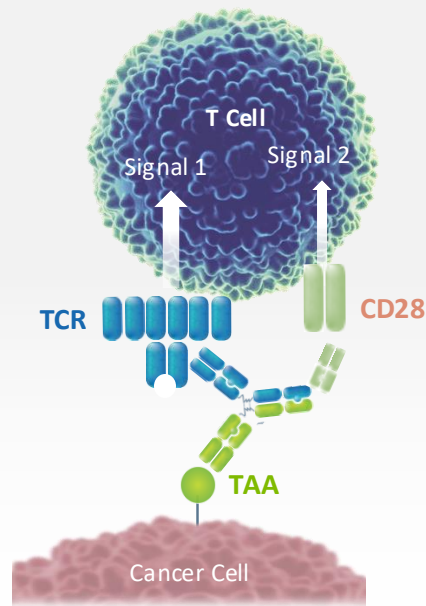
TriTCE Co-Stimulatory Therapeutic Program

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



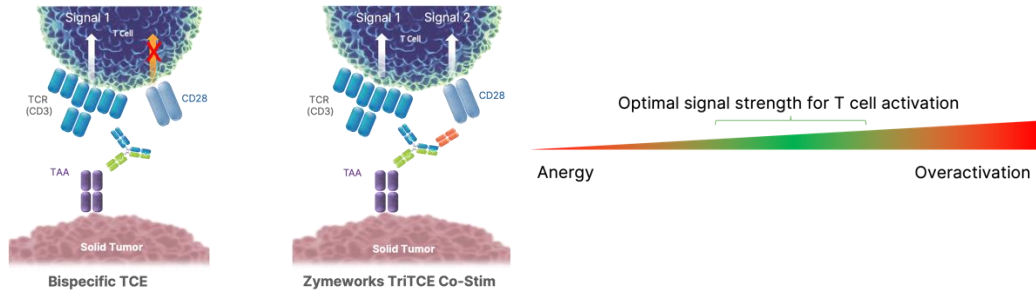
Provides Signal 1 (CD3) and Signal 2 (CD28) in one molecule to increase T cell activation and proliferation

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

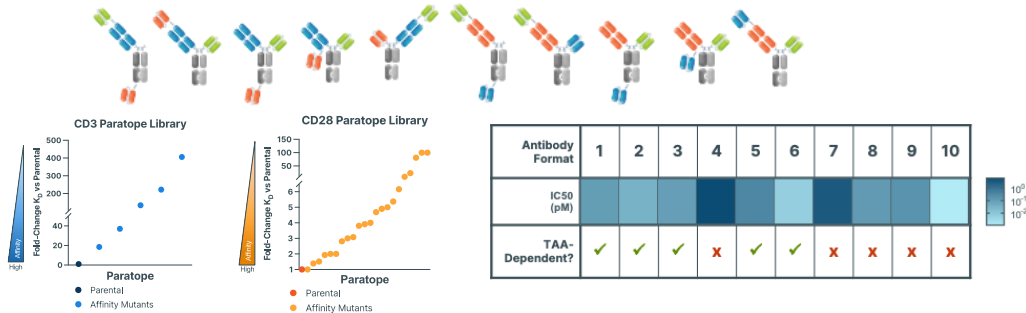
Novel Engineering and Screening Approach Identifies Co-Stimulatory Trispecifics with Greater Anti-Tumor Activity and Target-Dependent T Cell Activation

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



- 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

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

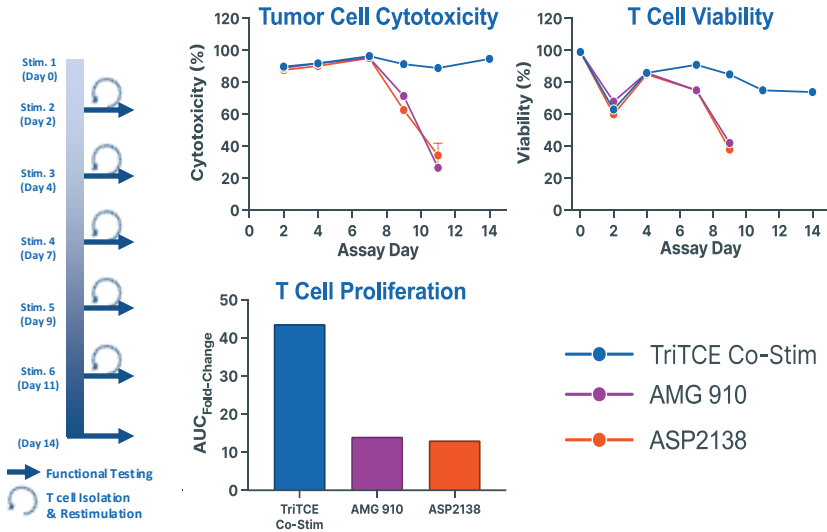


Neuhook L et al., TriTCE Co-Stim, next generation costimulatory trispecific T cell engagers for the treatment of solid tumors. Abstract #5121 presented at American Association for Cancer Research annual meeting 2023.

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

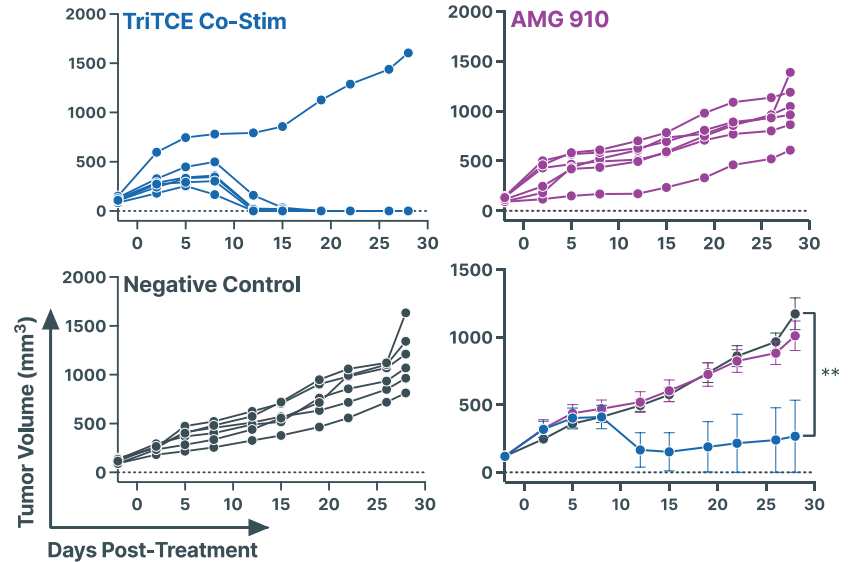
- Designed to enhance T cell activity and provide more durable anti-tumor control
- CLDN 18.2 used as a model tumor antigen and activity benchmarked against clinical stage bispecific TCEs

Sustained T cell Cytotoxicity and T cell Fitness



CLDN18.2 TriTCE Co-Stim displays sustained T cell fitness and anti-tumor activity in an established, repeat challenge assay. T cells were stimulated with SNUG03 cells (5:1 E:T) and restimulated (1:100). For each subsequent round of stimulation, T cells were isolated from the T cell culture medium, and re-stimulated with fresh SNUG03 target cells (5:1 E:T) at a fresh restim ratio (1:100). Schematic of T cell restimulation. T cell restimulation was assessed for tumor cell cytotoxicity, T cell viability, and T cell proliferation. Data are representative of two individual donors and are presented as mean \pm SEM. T cells for restimulation with AMG910 and ASP2138 were excluded for technical error (tumor cell cytotoxicity).

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



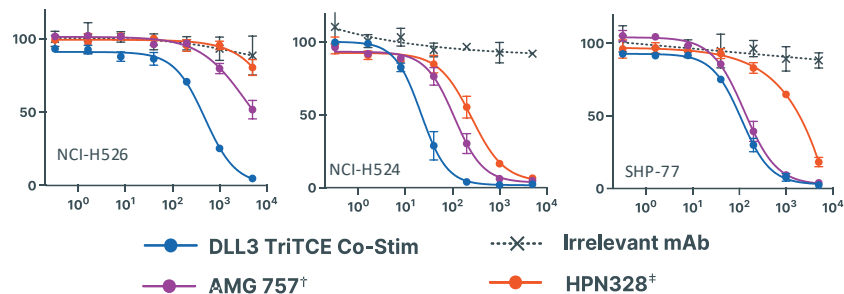
In vivo efficacy following treatment with CLDN18.2 TriTCE Co-Stim. NCG mice (n=6) were injected SC with SNUG03 (5x10⁶) target cells, engrafted with human PBMCs, and treated IV with 0.05 mg/kg of test article q3w x4. Mice were assessed for tumor volume. Data are presented as mean \pm SEM. ** p < 0.01.

E:T: Effector to Target ratio; NCG: nude, complement deficient, gamma-irradiated; PBMC: peripheral blood mononuclear cells; SC: subcutaneous.
AMG910 (CLDN 18.2/CD3 bispecific T cell engager) & ASP2138 (CLDN 18.2/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

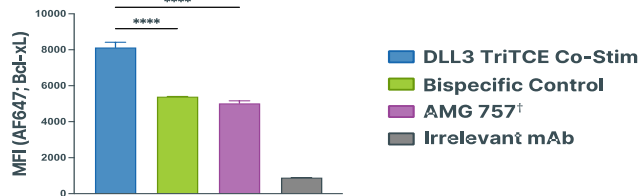
Designed to incorporate CD28 costimulation to improve activity beyond conventional DLL3xCD3 bispecifics by enhancing T cell activity and providing more durable responses in poorly infiltrated 'cold' tumors

Enhanced T Cell Cytotoxicity (SCLC)



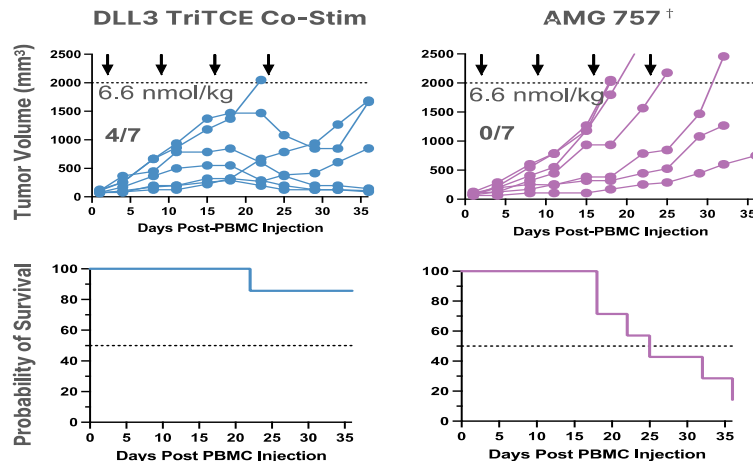
DLL3 TriTCE Co-Stim displays superior in vitro cytotoxicity relative to clinical benchmarks across multiple DLL3-positive SCLC tumor cell lines. Test articles were incubated with T cells co-cultured with DLL3-expressing tumor cell lines (E:T=1:2) for 7 days and evaluated for cytotoxicity.

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 NG-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 x4. 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. Competitors

Co-Stimulatory (CD28) TCE Strategies	Zymeworks' Potential Advantage and Limitations of Alternative Strategies
Zymeworks TriTCE Co-Stim	<ul style="list-style-type: none"> ✓ 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 primates³
CD28xTAA Bispecific (e.g. Regeneron, Xencor)	<ul style="list-style-type: none"> ❑ 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)	<ul style="list-style-type: none"> ❑ Increased development and challenging dose optimization requirements for two molecules¹³ ❑ Potential for CD28 bispecific irAEs⁹ ❑ Challenging TAA pairs or non-overlapping epitope targets requirements⁶
CD28xCD3xTAA Trispecific (Sanofi)	<ul style="list-style-type: none"> ❑ 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., JTC (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., BIP (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



Status

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



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

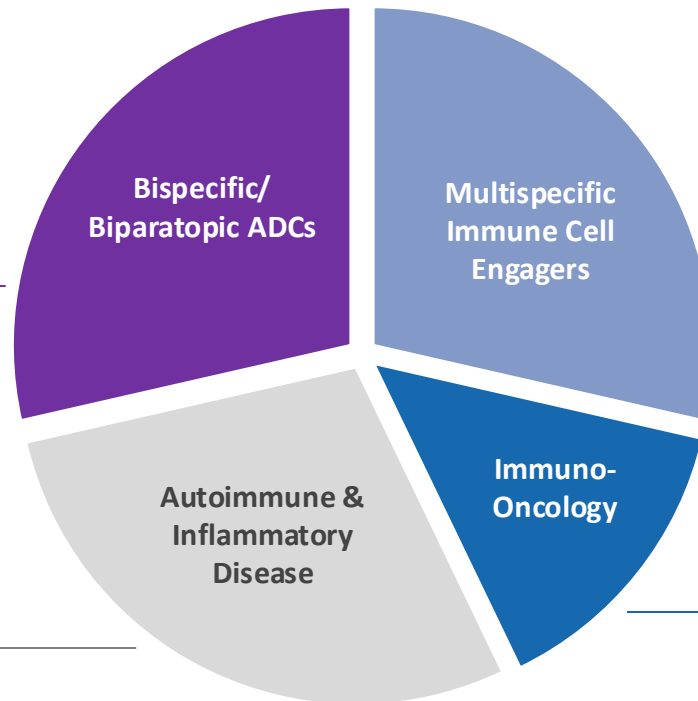
ADVANCE Portfolio Framework

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



Multispecific Cell Engagers

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

AIID

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

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

Current pipeline provides diversity and multiple opportunities for success with 5 novel therapeutics expected to be in active clinical trials 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™; EFFECT™; ProTECT™; ADC Platform includes cysteine insertion technology and novel payloads.

Milestone Opportunities in 2024 & 2025



Cash resources* as of
September 30, 2024 **\$374.9M**



Substantial potential milestone payments for
zanidatamab in GEA with further upside from
royalties and commercial milestones



Potential to nominate 2 candidates every
year from 2027+



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



Multiple value generating opportunities
expected in 2024 and 2025, with **5 novel
therapeutics expected to be in active
clinical trials by 2026**



- **Potential China approval** for
zanidatamab in 2L BTC during 2025
- **Pivotal Phase 3 top-line data readout
in GEA 1L** targeted by our partner Jazz
in 2Q 2025

*Includes cash, cash equivalents and marketable securities.

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