Zymeworks
Corporate Presentation

November 2022

NYSE: ZYME

www.zymeworks.com

Legal Disclaimer

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

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

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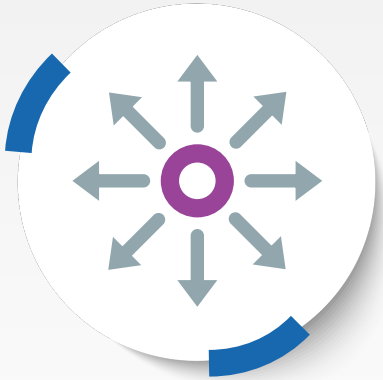
Multifunctional Antibody Therapeutics for Oncology



Paradigm Shift Towards Next-Generation ADCs and Multifunctional Therapeutics

The future of drug development lies in therapeutics that target diseases with multiple mechanisms of action

Leading the Next Wave of Multifunctional Therapeutics

Zymeworks is at the forefront of this paradigm shift by developing multifunctional therapeutics through its proprietary platforms

Fully-Integrated R&D Pipeline from Target Selection through Pivotal Studies

Employee base with experience to discover, develop, and commercialize our novel agents globally with partners and collaborators

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Focused R&D to Help Drive Next Wave of Development for Difficult-to-Treat Cancers

Integrated R&D Engine

- Multispecific Antibody Therapeutics (MSAT)
- Antibody Drug Conjugates (ADC)

Product Profile

- First and Second-line market opportunities
- Accelerated Approval regulatory pathway allows potential of early market entry

Focus on indications with worst patient prognosis (e.g., 5-year OS)

Pursue lead indications with global peak sales potential **>$500MM** per product

ADC: antibody-drug conjugate; IND: investigational new drug application; OS: Overall Survival

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Novel Platforms Enable Unique and Differentiated Multifunctional Therapeutics

Platforms Driving the Next Generation of Antibody Based Therapeutics

Azymetric™

Multispecific Antibody Generation

- Biparatopic/Bispecifics
- Trivalent/Trispecifics
- T-cell engager technology
- Fc-Fusions
- IgG1-like biophysical, manufacturing, and purification protocols

Drug Conjugate Platforms

Fit-For Purpose ADC Candidate Creation

- ZymeLink™ Auristatin
- ZymeLink™ Hemiasterlin
- TOPO1i Technology
- Cysteine-Insertion Conjugation Technology
- Immune Stimulating (TLR7)

EFECT™

Tailored Immune Function Modulation

- Tailored sets of Fc modifications that can modulate immune cell recruitment and function
- Enhance or eliminate immune effector function to optimize therapeutics

ProTECT™

Tumor-Specific Immune Co-stimulation

- Tumor-specific activity via conditional blocking to reduce off-tumor toxicities
- Functional block adds co-stimulation or checkpoint modulation to enhance efficacy

Enable New Biology | **Modular** | **Scalable**

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Clinically Proven: Zymeworks Technology Platforms Yield Therapeutics

Multispecific

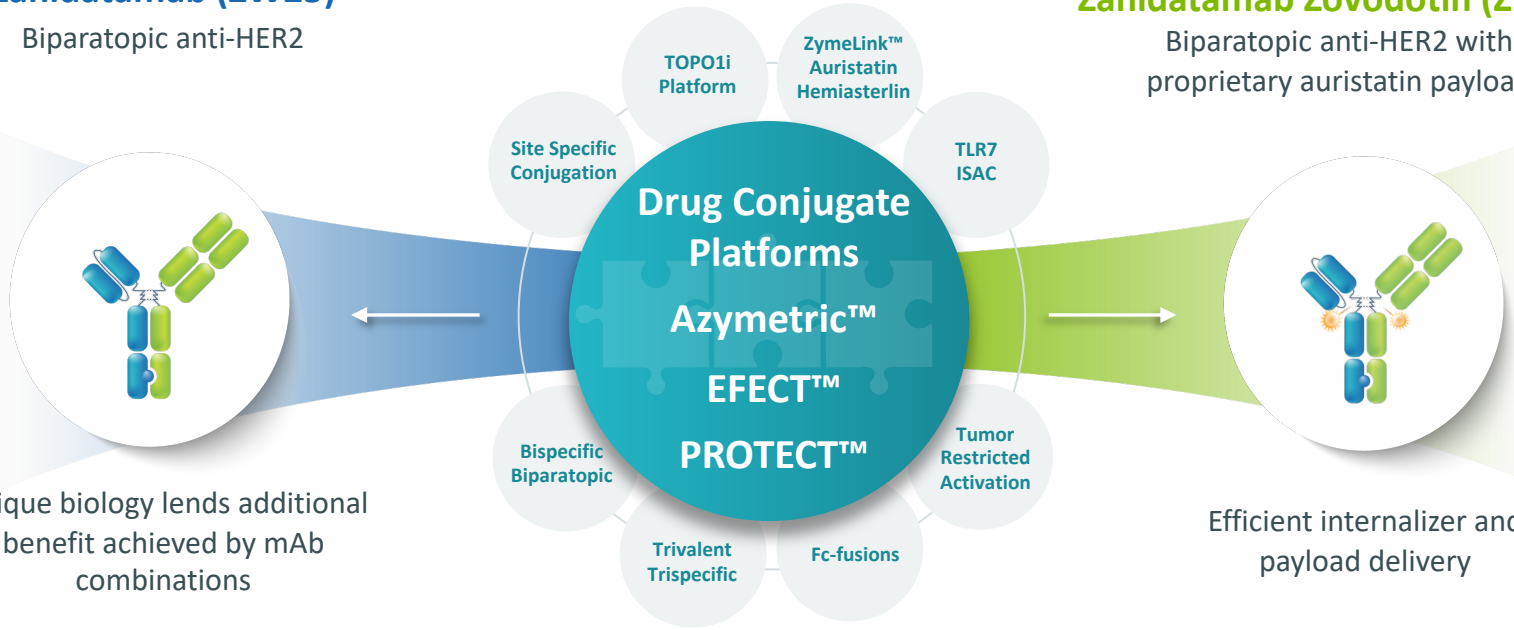
Zanidatamab (ZW25)

Biparatopic anti-HER2

Antibody Drug Conjugate

Zanidatamab Zovodotin (ZW49)

Biparatopic anti-HER2 with proprietary auristatin payload



Unique biology lends additional benefit achieved by mAb combinations

Efficient internalizer and payload delivery

Pivotal clinical studies

Goal of 5 New INDs in 5 years

Clinical POC study

DAR: drug to antibody ration; Fc: fragment crystallizable region of antibody; HER2: human epidermal growth factor receptor 2; IND: investigational new drug application; ISAC: Immunostimulatory Drug Conjugate; MOA: mechanism of action; POC: proof of concept

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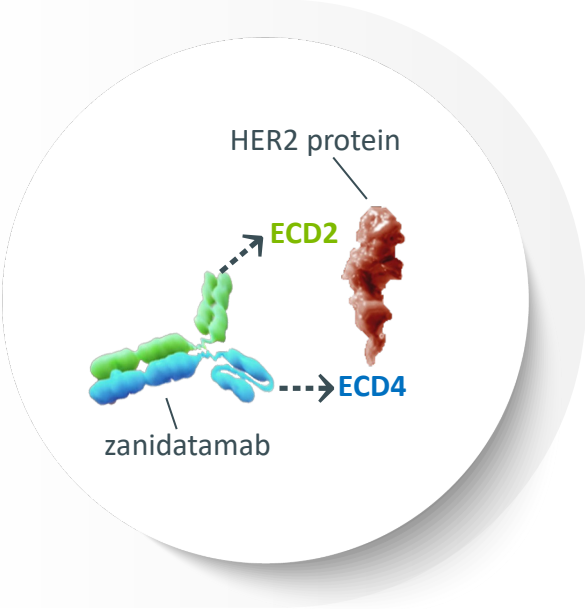
A Growing Product Candidate Pipeline of Potential Best-in-Class Therapeutics

PROGRAMS | COMMERCIAL RIGHTS	TARGET	LATE-DISCOVERY	IND-ENABLING	PHASE 1	PHASE 2	MILESTONE
LEAD PRODUCT CANDIDATES						
Zanidatamab *HER2 X HER2 Bispecific* *Jazz Pharmaceuticals **BeiGene	HER2	Biliary Tract Cancer | *FDA Breakthrough Therapy designation* | HERIZON-BTC-01			HERIZON	
	HER2	Gastroesophageal Adenocarcinomas | HERIZON-GEA-01			HERIZON	
	HER2	Breast Cancer				
	HER2	HER2-Expressing Solid Tumors				
Zanidatamab Zovodotin (ZW49) *HER2 X HER2 Bispecific ADC* zymeworks **BeiGene	HER2	HER2-Expressing Solid Tumors				
PRECLINICAL PROGRAMS						
ZW191 *TOPO1i ADC*	FRα	OVCA, Gynecological, NSCLC				**IND: 2024**
ZW171 *2+1 CD3-Engager*	MSLN	OVCA, Pancreatic, CRC				**IND: 2024**
ZW220 *TOPO1i ADC*	NaPi2b	OVCA, NSCLC				Pilot NHP toxicology study initiated
ZW251 *TOPO1i ADC*	GPC3	Hepatocellular Carcinoma				Pilot NHP toxicology study initiated

*Jazz to develop and commercialize across all indications in the United States, Europe, Japan.
**BeiGene to develop and commercialize in Asia Pacific countries including China, South Korea, Australia, and New Zealand (excluding Japan).

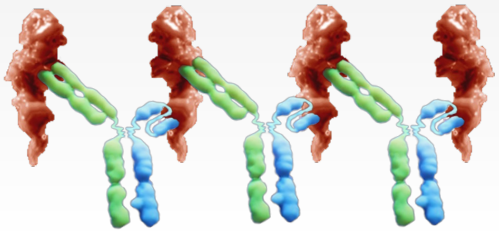
Zanidatamab: A Bispecific Antibody for HER2-Expressing Cancers



Zanidatamab's Unique Binding Geometry Promotes:

- Biparatopic – targets two distinct HER2 epitopes and results in HER2 binding across a range of expression levels (low to high)
- HER2-receptor cross-linking, clustering, internalization, and downregulation
  - Enhanced receptor clustering on cell surface (cluster internalization, receptor downregulation)
  - Inhibition of cellular proliferation
- Fc-mediated cytotoxicity: ADCC, ADCP, CDC

Dual HER2-Binding of Zanidatamab Drives Unique MOA



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

Note: Zanidatamab has been granted Breakthrough Therapy designation by the FDA for patients with previously-treated HER2 gene-amplified BTC as well as two Fast Track designations, one for previously treated or recurrent HER2-positive BTC and another for first-line 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 in the European Union.
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

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Zanidatamab: Developed Internally with ZYME Protein Engineering Expertise

2013 - 2014

- First biparatopic anti-HER2 antibody expressed
- Cell-line development started

2016

- IND accepted by FDA
- First patient dosed in Phase 1 clinical trial

2018

- First clinical data presented at ASCO
- Zymeworks and BeiGene announced license and collaboration agreement for zanidatamab in APAC region

2019

- Initiated first Phase 2 clinical trial in 1L GEA
- Zanidatamab granted Fast Track and Orphan Drug designation by FDA

2020

- Initiated pivotal trial in advanced HER2-amplified BTC
- Zanidatamab receives Breakthrough Therapy Designation in BTC
- Phase 1 data in GEA presented at ASCO GI

2021

- Initiated global Phase 3 pivotal in 1L GEA

2022

Announces Global Licensing Agreement[1] with Jazz Pharmaceuticals

APAC: Asia Pacific; ASCO: American Society of Clinical Oncology Annual Meeting; BTC: Biliary Tract Cancer; FDA: US Food and Drug Administration; GEA: gastroesophageal adenocarcinoma; IND: investigational new drug application

[1] Excludes commercial territories in Asia Pacific countries controlled by BeiGene

Key Financial Terms of Licensing Agreement with Jazz

	Licensing Agreement Terms[1]
Counterparty	Jazz Pharmaceuticals
Upfront Payments[2]	$375,000,000
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[3]
Future R&D Spend	Jazz to fund 100% of costs of future studies

Additional Details:

- Upfront payments[2] reflect $50MM one-time payment upon receipt of HSR Clearance and, at Jazz's option, $325MM after top-line HERIZON-BTC-01 data
- Ongoing zanidatamab related clinical studies and initial BLA to be managed by Zymeworks (100% of costs reimbursed)
- Future zanidatamab-related clinical studies, regulatory filings and commercialization to be managed and funded by Jazz
- Jazz to have exclusive license in US, EU, Japan and all other territories except those in Asia Pacific not covered by BeiGene agreement
- Zymeworks will continue to supply zanidatamab to Jazz for clinical and commercial use for at least two years (100% of costs reimbursed)

[1] All dollar values in US Dollars
[2] Zymeworks is eligible to receive a $50 million upfront payment, following receipt of the clearance relating to the United States Hart-Scott Rodino Antitrust Improvements Act of 1976 (such clearance, the "HSR Clearance"), and should Jazz decide to continue the collaboration following readout of the top-line clinical data from HERIZON-BTC-01, a second, one-time payment of $325 million
[3] Costs related to ongoing clinical studies incurred after signing of the agreement to be reimbursed 100% by Jazz

Key Benefits to Zymeworks of Zanidatamab Licensing Agreement

- **Meaningful improvement** to **financial position** and **reduction in future expenditures** allow Zymeworks to focus on growth of exciting early-stage pipeline while zanidatamab advances to commercialization
- **Accelerate and expand R&D programs** (early R&D and ZW49) 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

Transaction allows zanidatamab to reach a broad group of patients globally and may potentially improve patient outcomes beyond the current standards of care

Key Financial Terms of Asia Pacific Licensing Agreement with BeiGene

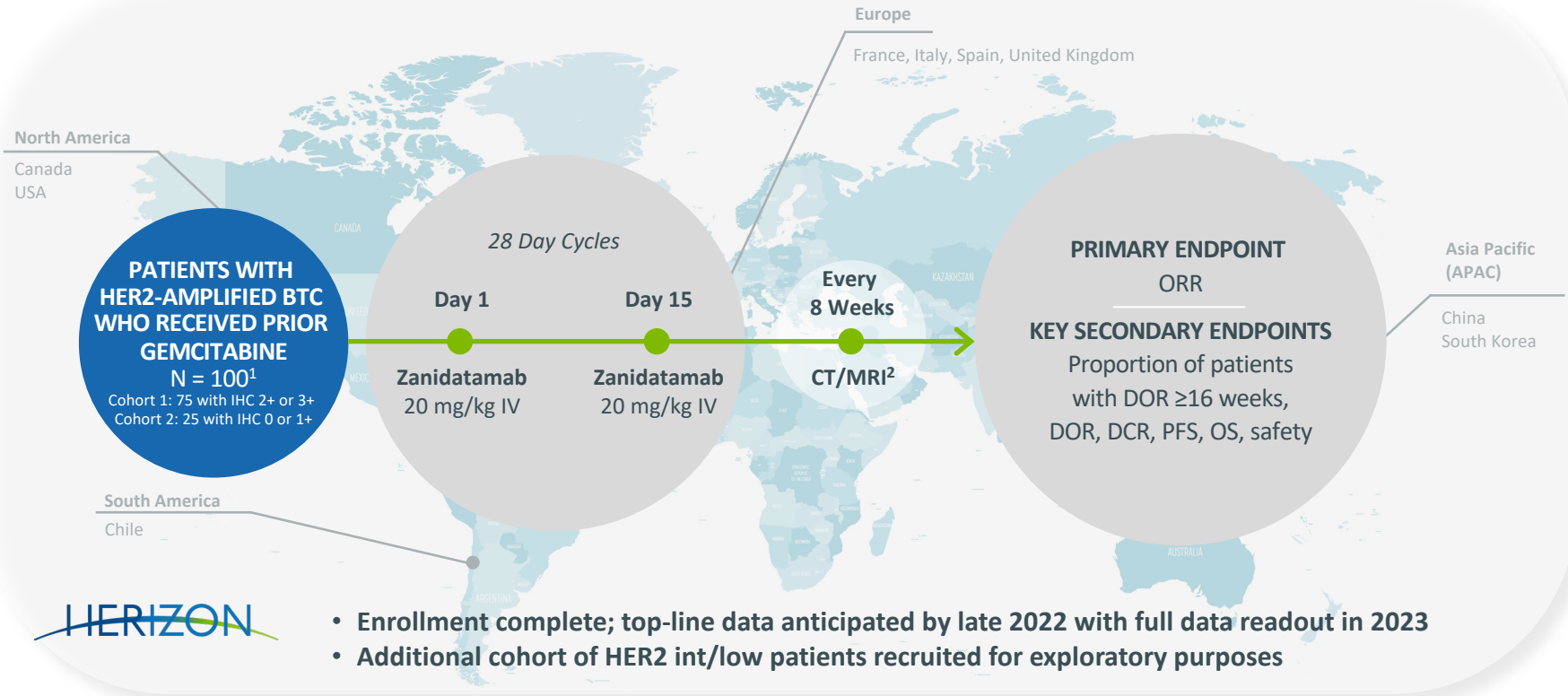
	Licensing Agreement Terms[1]
Counterparty	BeiGene
Upfront Payments	$40,000,000
Development and Commercial Milestones	Up to $390,000,000
Royalties	Tiered royalties on up to 20% of net sales in BeiGene territories
Co-development Funding	Currently for BTC and GEA global development

Additional Details:

- Received $40MM upfront payment in 2018 and $20MM in milestones to-date
- BeiGene has development and commercial rights to zanidatamab and ZW49 in Asia-Pacific region (excluding Japan and India)
- 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

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



HERIZON

- **Enrollment complete; top-line data anticipated by late 2022 with full data readout in 2023**
- **Additional cohort of HER2 int/low patients recruited for exploratory purposes**

BTC: biliary tract cancer; DCR: disease control rate; DOR: duration of response; IHC: immunohistochemistry; IV: intravenous; MRI: magnetic resonance imaging; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; Q2W: every 2 weeks; RECIST: Response Evaluation Criteria in Solid Tumors.

[1]All patients on study are HER2-amplified as determined by in-situ hybridization (ISH) assay.

[2]For tumor assessment per RECIST v1.1.2.

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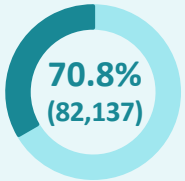
Epidemiology of Biliary Tract Cancer

- Biliary Tract Cancers (BTC) are molecularly diverse tumours which include gallbladder cancer (GBC), intrahepatic cholangiocarcinoma (IHCC), and extrahepatic cholangiocarcinoma (EHCC)[1]
- Gall bladder cancer is 80-95% of biliary tract cancer cases[2]

Epidemiology (World)

Incidence varies globally:

- GBC accounts for **0.6%** of all adult cancers **worldwide** (~116,000 new cases in 2020)[3,4]



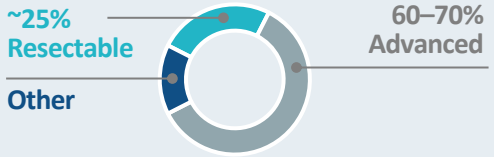
of all estimated new gallbladder cancer cases occurred in Asia in 2020[4]

- In 2017, by country, **Chile** had the highest BTC incidence worldwide, followed by Japan and South Korea (10.83, 8.88, and 8.55/100,000, respectively)[5]
- **~10%** of all estimated new gallbladder cancer cases (12,570) occurred in **Europe in 2020**[4]

Epidemiology (United States)

Most cases are diagnosed at an advanced stage:

CASES BY STAGE AT DIAGNOSIS[6,7]



~7,500 new cases of BTC diagnosed annually in the US[8]

Progression Considerations

Second line:

- 15-44% of patients receive 2L treatment in Western trials; 75-82% receive 2L in Japan trials[9,10]
- 2L chemotherapy yields response rates of < 10%; median overall survival of patients is often < 6 months[11] with a recent phase II trial reporting 8.6 months[12]
- ~40-60% of BTC patients present possible targetable alterations with differences between anatomical subgroups[6,13]

19% of GBC
17% of EHCC
5% of IHCC
} Overexpress HER2[14]

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.GLOBOCAN. Gallbladder fact sheet. 2020. 4.GlOBOCAN. World fact sheets. 2020; 5.Zhang Y et al., Cancer Epidemiology. 2021; 6.Gómez-España MA, et al., Clin Transl Oncol. 2021; 7.Banales JM et al., Nat Rev Gastroenterol Hepatol. 2020; 8.NCI. SEER. SEER*Explorer: Pancreatic & Biliary Cancer. 2021; 9.Chiang N-J et al., Biomolecules. 2021; 10. Fornaro L et al., Br J Cancer. 2014; 11.Lamarca A et al., J Clin Oncol. 2019; 12.Yoo C et al., Final results *(NIFTY)* abstract 55P presented at ESMO Congress 2022; 13.Bridgewater JA et al., Am Soc Clin Oncol Educ Book. 2016; 14.Galdy S et al., Cancer Metastasis Rev. 2017

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Targeted Treatment Options are Rapidly Evolving in Biliary Tract Cancer

Advanced / Metastatic Biliary Tract Cancer

First-Line Treatment Options

SOC based on ABC-02 trial (Global):
Gemcitabine + Cisplatin
mPFS = 8.4 months, mOS = 11.7months[1]

SOC option with TOPAZ-1 trial (United States):
Cisplatin + Gemcitabine + Durvalumab
mPFS= 7.2months, mOS = 12.9 months[2]

Progression in Metastatic Biliary Tract Cancer

Second-Line Treatment Options

SOC based on ABC-06 trial (Global):
FOLFOX mPFS= 4.0months, mOS = 6.2months[3]

Is Targeted Treatment More Effective Than Chemotherapy?

FGFR2 fusions or rearrangements mPFS = 7.0 months, mOS = 17.5 months[4]
IDH1 mutation, mPFS = 2.7 months, mOS = 10.3 months[5]

Results from HER2 Targeting Agents in 2L+ Trials *

Trastuzumab + FOLFOX mPFS = 5.1months, mOS = 10.7 months[6]
TDXd (HERB trial) mPFS = 5.1months, mOS = 7.1 months[7]
Trastuzumab + Pertuzumab (MyPathway) mPFS = 4.0, mOS = 10.9 months[8]

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)[9]

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, fibroblast growth factor receptor 2; 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; SOC, standard of care; TDXd, trastuzumab deruxtecan . * have not received FDA (or any regulatory authority) approval for BTC 2L indication

1. Valle J et al., New Engl J Med 2010; 2. Oh et al., updated at ESMO 2022; 3. Lamarca et al., J Clin Oncol 2019; 4. Vogel A et al., Updated at ESMO 2022; 5. Abou-Alfa GK et al., Lancet Onc 2020; 6. Lee C-K et al., Lancet Gastroenterol Hepatol 2022; 7. Ohba A et al., J Clin Oncol 2022; 8. Javle M et al., Lancet Oncol 2021. 9 Valle JW et al., Lancet 2021

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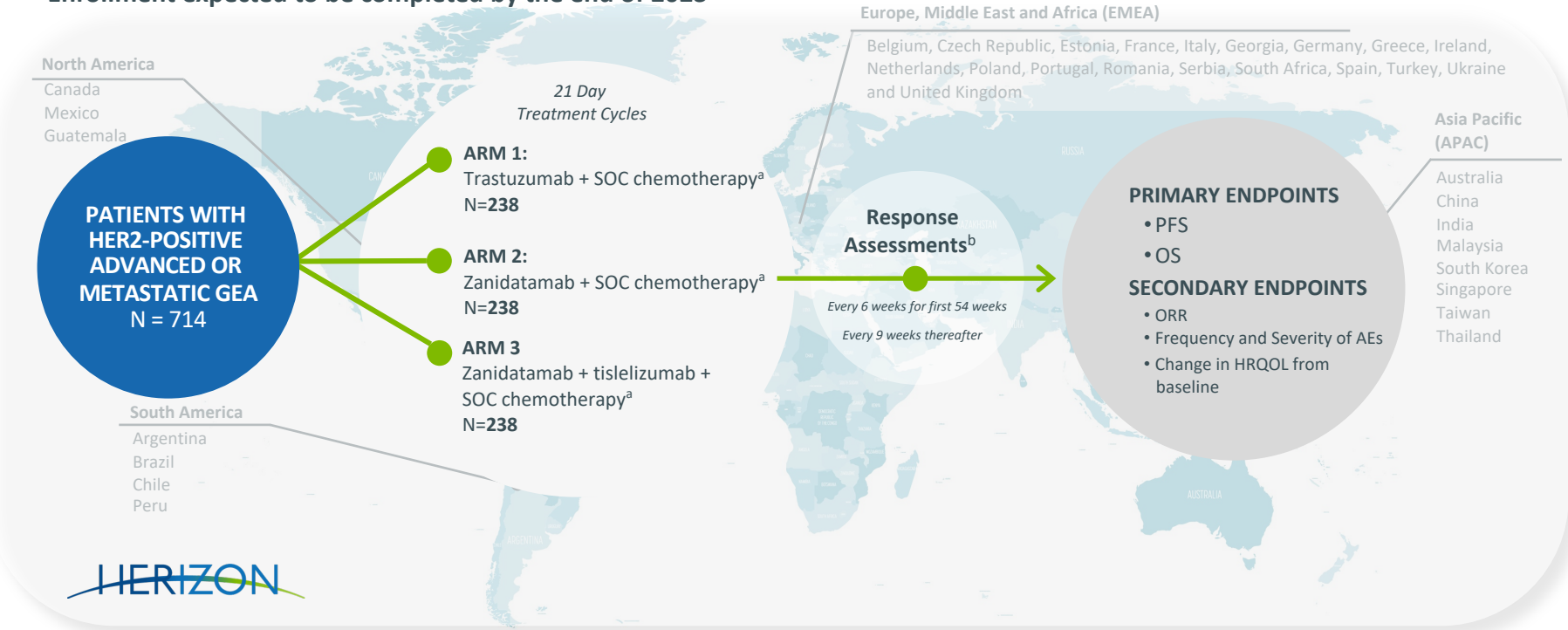
HERIZON-GEA-01: A Global Pivotal Study in First-Line HER2-Positive GEA

- **Study plans to enroll 714 patients at approximately 300 sites across more than 30 countries**
- **Enrollment expected to be completed by the end of 2023**

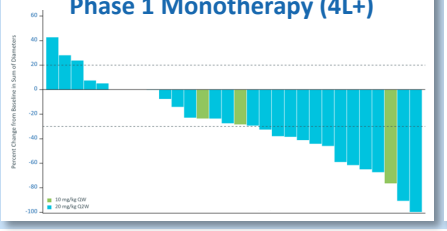


[a] SOC (standard of care) chemotherapy: CAPOX or FP; [b] response assessments until progression per BICR or withdrawal of consent
BICR: Blind independent central review; GEA: gastroesophageal adenocarcinoma; PFS: Progression-free survival; OS: overall survival

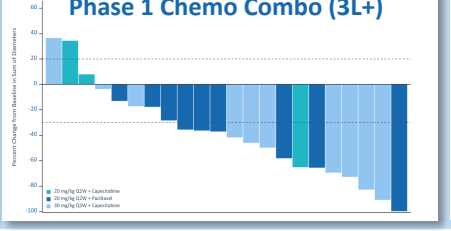
Upcoming Zanidatamab Clinical Catalysts

Gastroesophageal

Phase 1 Monotherapy (4L+)



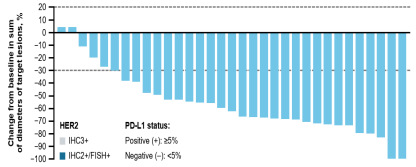
Phase 1 Chemo Combo (3L+)



Phase 2 Chemo Combo (1L)

1H 2023[1]

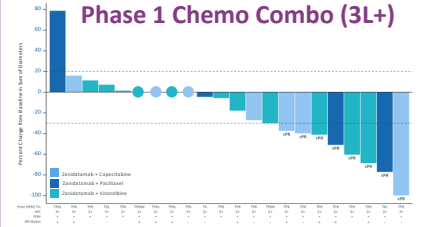
Phase 2 Tisle + Chemo Combo (1L)



Breast Cancer

Phase 1 Monotherapy (Late-Line)

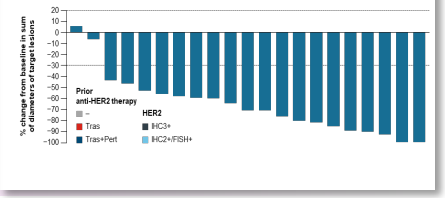
Phase 1 Chemo Combo (3L+)



Phase 2 CDK4/6 Combo (3L+)

4Q 2022[2]

Phase 2 Chemo Combo (1L)

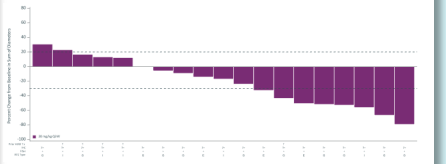


BTC & Others

Other Cancers: Phase 1 Monotherapy (Late-Line)

4Q 2022[3]

BTC: Phase 1 Monotherapy (2L+)



BTC: Phase 2 Chemo Combo (1L)

Currently Enrolling

BTC: Phase 2 Registrational Trial (2L)

4Q 2022[4]

Breast Cancer: Phase 1 Monotherapy (Late-Line), Phase 1 Chemo Combo (3L+), Phase 2 Chemo Combo (1L)
Other Solid Tumor: BTC Phase 1 Monotherapy (2L+), Others: Phase 1 Monotherapy (Late-Line)

[1] Updated data, initially presented at ESMO in 2021, is anticipated to be presented in the first half of 2023 [2] Data anticipated to be presented in the fourth quarter 2022; [3] Manuscript anticipated to be published in the fourth quarter 2022; [4] Topline data expected to read out 4Q22

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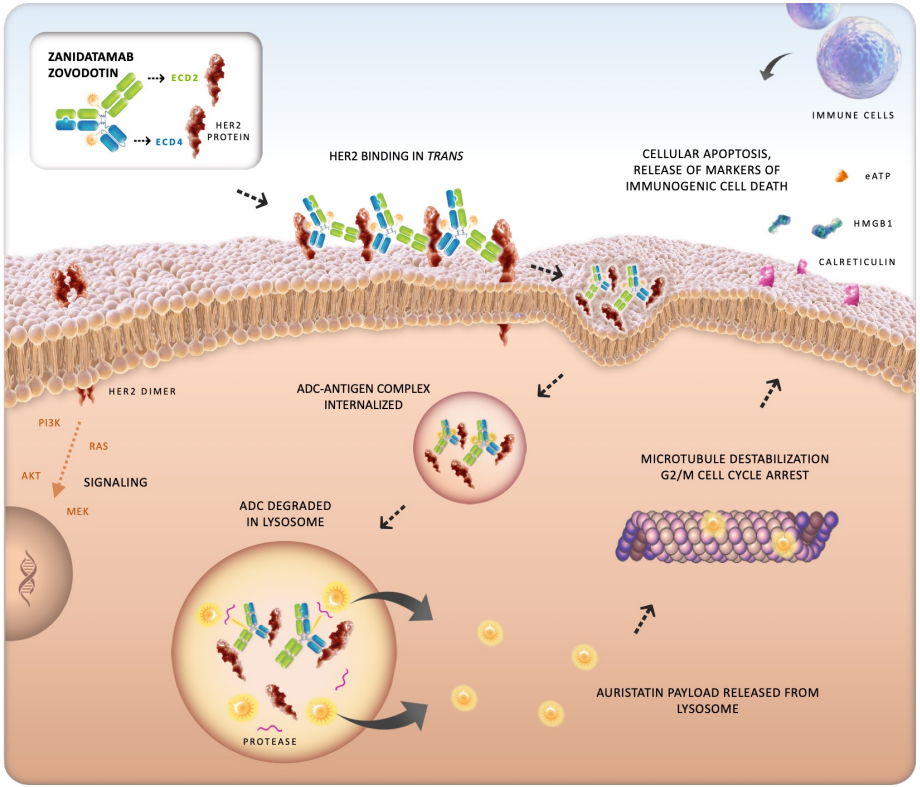
Zanidatamab Zovodotin: A Bispecific ADC for HER2-Targeted Therapy

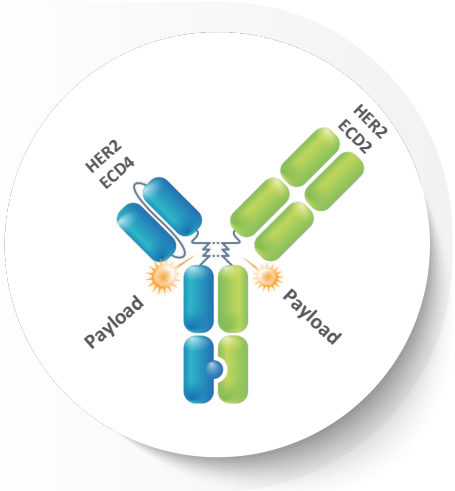
Unique Mechanism of Action[1,2,3]

- IgG1-like biparatopic antibody backbone directed against ECD4 & ECD2 of HER2
- Antibody sequence identical to zanidatamab
- Proprietary auristatin payload covalently linked to the antibody via a protease-cleavable linker
- Average drug-to-antibody ratio (DAR) of 2
- Biparatopic antibody-induced internalization with increased auristatin-mediated cytotoxicity and immunogenic cell death
- Potential to address unmet need in cancers with high and low levels of HER2 expression and HER2-mutations



ADC, antibody-drug conjugate; AKT, serine-threonine protein kinase family; eATP, extracellular adenosine 5′-triphosphate; ECD, extracellular domain; HER, human epidermal growth factor receptor; HMGB1, high mobility group box 1; G2/M, second gap phase/mitotic phase; MEK, mitogen-activated protein kinase kinase; PI3K, phosphatidylinositol 3-kinase; RAS, rat sarcoma pathway 1. Hamblett et al., #3914 Poster Presentation at AACR 2018; 2. Davies et al., #3912, Poster Presentation at AACR 2018; 3. Data on file

Zanidatamab Zovodotin: A Bispecific ADC for HER2-Targeted Therapy



Zanidatamab Zovodotin Data Highlights and Catalysts

Clinical Data Highlights

- Differentiated tolerability profile amongst HER2-targeted ADCs with the majority of adverse events being grade 1 or 2 and manageable
- Confirmed ORR of 31%, disease control rate of 72% observed across 29 response-evaluable patients treated with zanidatamab zovodotin at 2.5 mg/kg Q3W
- Clear single-agent activity in heavily pretreated patients with potential go-forward regimen of 2.5 mg/kg dosed every three weeks
- Weekly dosing regimen continues to enroll with dose escalation at 1.75 mg/kg and an expansion cohort at 1.5 mg/kg

Expected Catalysts

- Update on progression of weekly expansion and escalation cohorts
- Recommended Phase 2 dose to be announced 4Q22

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

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022; ORR: objective response rate

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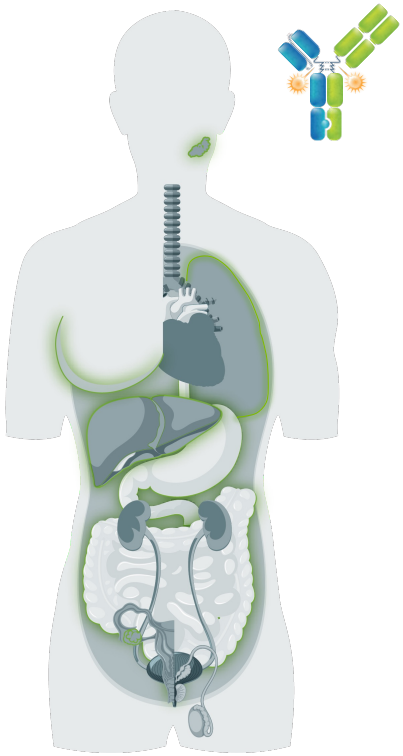
Zanidatamab Zovodotin: Differentiated HER2-Targeted ADC



Zanidatamab zovodotin

has shown single-agent activity in multiple tumor types with a differentiated tolerability profile amongst other HER2-targeted ADCs and has multiple pathways for development

Non-Small Cell Lung Cancer (NSCLC)

HER2-amplified, -expressing, and -mutated

Metastatic Breast Cancer (mBC)

HER2-positive mBC after previous treatment with T-DXd

HER2-low mBC

Gastroesophageal Adenocarcinoma (GEA)

Previously treated HER2-positive GEA

Other HER2-expressing Tumors

Ovarian, endometrial, bladder

DIFFERENTIATED STRATEGY

Differentiated tolerability profile with no interstitial lung disease, no significant neuropathy, and no significant neutropenia noted to date

Single-agent activity across multiple HER2-expressing tumor types

Potential combinability with standards of care across indications, with no known overlapping toxicities

Incrementally staged investment in clinical development to **preserve and maintain** cash runway

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022

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Legacy Partnerships & Collaborations Validate Zymeworks' Technology

PROGRAMS | PLATFORMS	PRECLINICAL	PHASE 1	PHASE 2	COMMERCIAL RIGHTS
PARTNERSHIPS				
Bispecific Antibody	Oncology			Bristol Myers Squibb*
XB002 (*ICON-2*) Tissue Factor ADC	Solid Tumors			EXELIXIS**
JNJ-78278343 CD3 x KLK2 Bispecific	Castration-Resistant Prostate Cancer			Johnson & Johnson INNOVATION
JNJ-78306358 CD3 x HLA-G Bispecific	Solid Tumors			Johnson & Johnson INNOVATION
ATRC-301 EphA2 Targeting ADC	Oncology			ATRECA
Bispecific Antibody	Undisclosed			MERCK
Bispecific Antibody	Immuno-Oncology			Daiichi-Sankyo
Bispecific Antibody	Infectious Disease/Undisclosed			gsk
Bispecific Antibody	Dermatology			LEO
Bispecific Antibody	Undisclosed			BeiGene

Azymetric EFECT ZymeLink

*Original Agreement with Celgene (which is now a Bristol-Myers Squibb company)
**Original Agreement with Iconic; XB002 in-licensed by Exelixis

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Zymeworks: Leading the Next Wave of BioTherapeutics

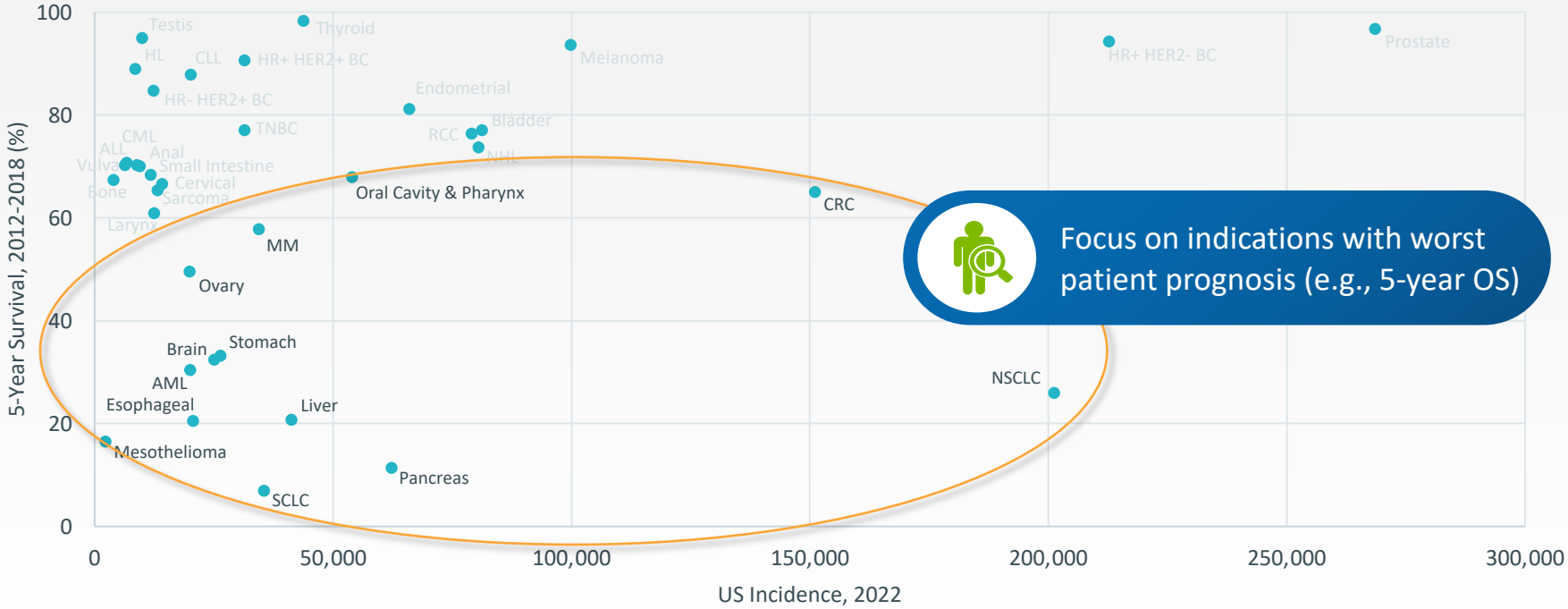
2017-2022

- Select Product Pipeline
- Platform Technologies & Tools
- Broad Platform Partnerships

2022-2027

- Increase In-House Pipeline
- Balance of ADCs and Multispecifics
- Maintain Technology Edge
- Select Product Partnerships

Cancer Indications with Greatest Unmet Patient Need



SEER*Explorer, accessed 10 Oct 2022

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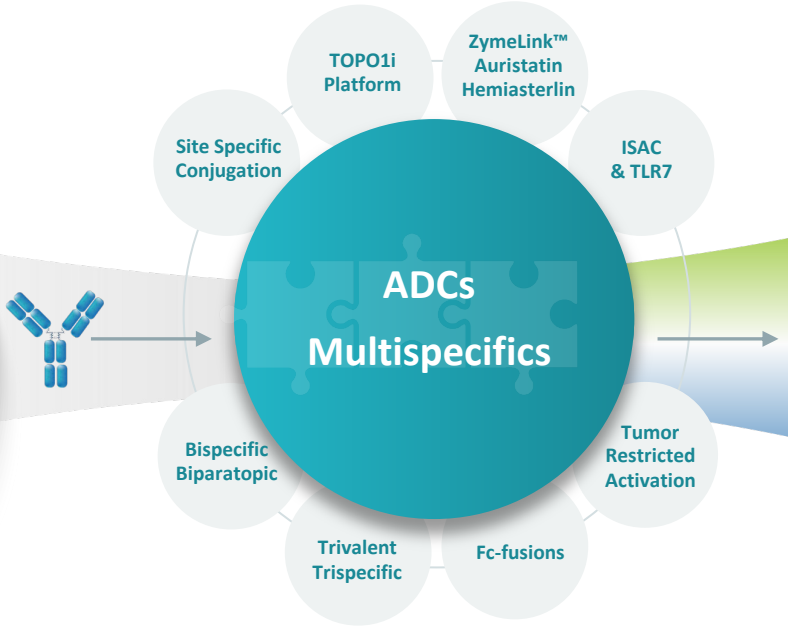
ADC and Multispecific Modalities Driving Our Pipeline

Select Difficult-to-Treat Tissue & Target

Design with Complementary Technology Platforms



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

ADC, antibody drug conjugate; DAR, drug to antibody ration;; Fc: fragment crystallizable region of antibody; ISAC, Immunostimulatory Drug Conjugate; MOA, mechanism of action

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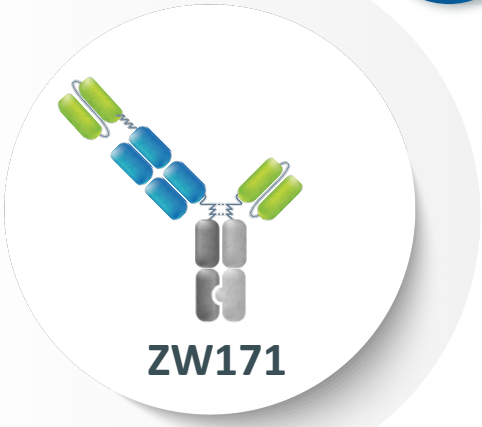
Zymeworks Multispecific T Cell Engager Strategy: Utilizing Azymetric™ to Build Differentiated & Next Generation Multispecific T Cell Engagers

Biological Problem	Zymeworks Solution
1 Narrow therapeutic window and toxicity due to CRS associated with Gen 1 TCE in solid tumors	**2+1 T Cell Engager (ZW171)** Mitigate CRS with low affinity T cell binding and enhanced efficacy and selectivity with avidity-driven tumor antigen binding
2 Limited T cell intratumoral availability and T cell anergy in solid tumors	**TriTCE Co-stimulation** Increase T cell fitness, activation and proliferation via tumor-dependent T cell co-stimulation
3 Immunosuppressive tumor microenvironment limiting T cell responses in solid tumors	**TriTCE Checkpoint Inhibitor** Increase T cell responses through simultaneous checkpoint blockade and avidity-driven binding

CRS: cytokine release syndrome; TCE: t cell engager

ZW171: 2+1 Bispecific MSLN x CD3 T Cell Engaging Antibody

Lead Preclinical Product Candidate



CD3
MSLN

MSLN Targeted

Antibody targets mesothelin (MSLN), a glycoprotein that is elevated in many cancers including pancreatic, mesothelioma and ovarian cancer

Target is clinically validated, indications have high unmet clinical need

CD3 Targeted

Targeting CD3 receptor to redirect T cell cytotoxicity towards cancerous cells

Anti-CD3 antibody targeting novel epitope that mediates low T cell binding and cytokine release and potent tumor cell lysis

Format Engineering

Extensive assessment of different formats with different valences & geometries

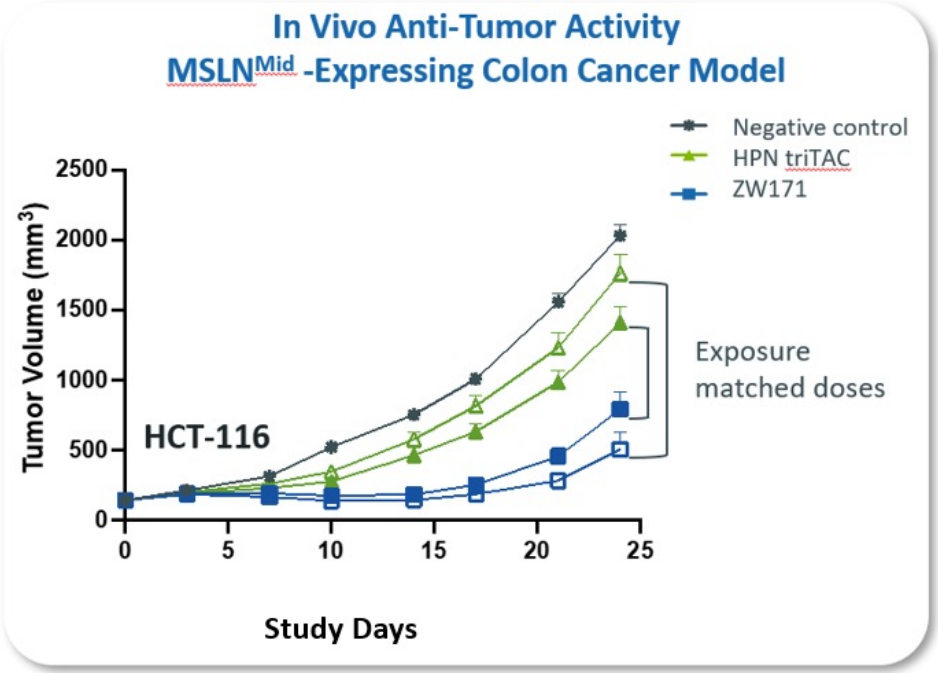
2+1 dual scFv identified as avidity-driven format with optimal activity and safety profile

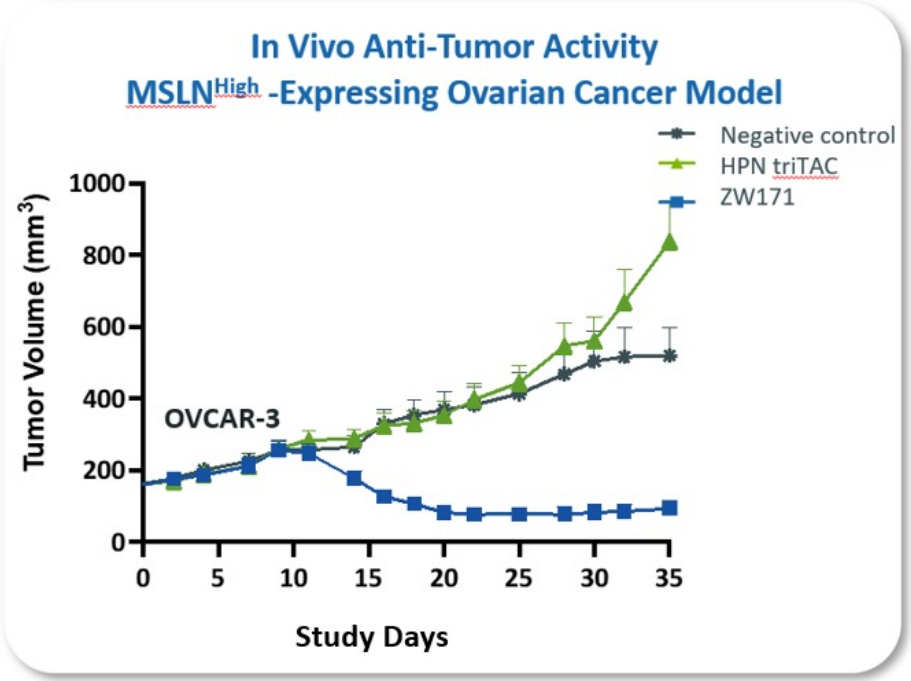
Validation

In preclinical development

IND 2024

ZW171 Mediates Greater In Vivo Anti-Tumor Activity Compared to Benchmark





NPG mice were engrafted with HCT116 cells and human PBMC (2 donors) intraperitoneally. When tumors reached 100-200 mm³, dosed i.v. QW x4 with ZW171 or i.p. daily x 18 with HPN triTAC. Serum exposure concentrations and matched exposure doses confirmed by PK analysis. Negative control is anti-hemagglutinin x CD3 bispecific.

OVCAR-3 tumor fragments were engrafted subcutaneously in NOG mice. After tumors reached 100-200 mm³, 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. Negative control is anti-hemagglutinin x CD3 bispecific.

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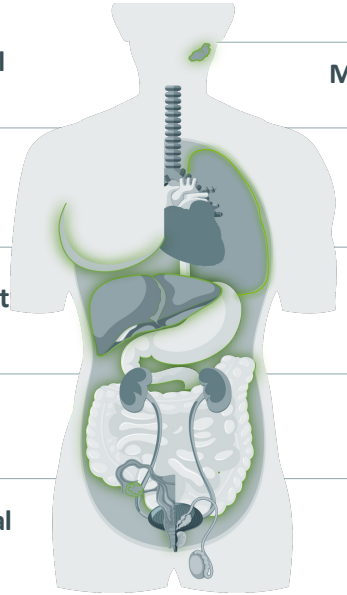
ZW171 Treatment Opportunity

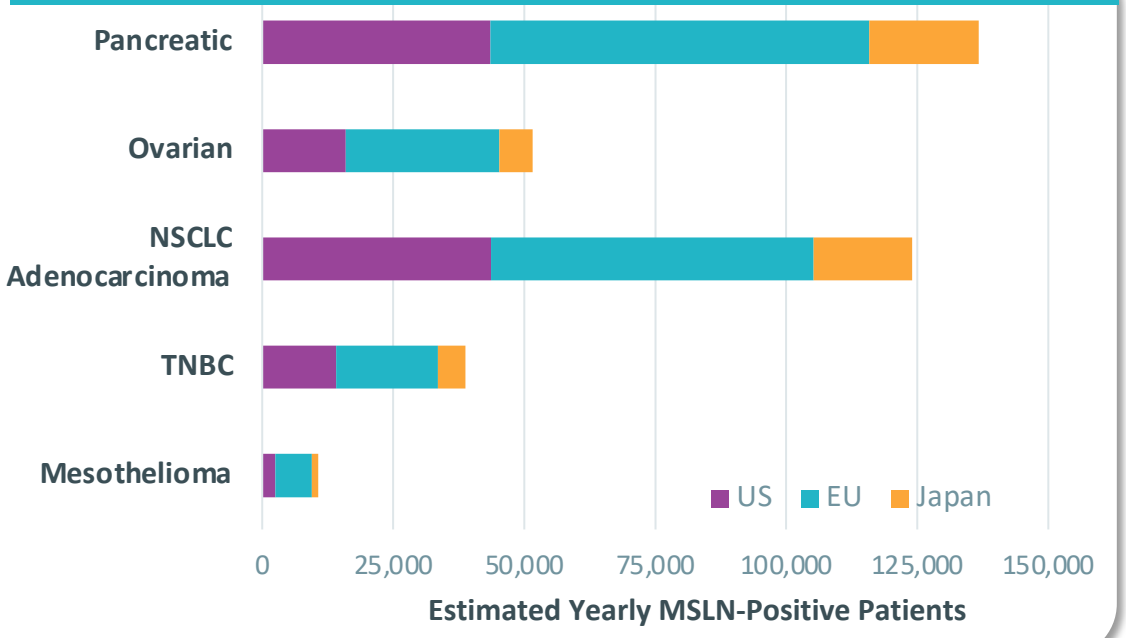
- Potential first and best-in-class treatment for MSLN+ pancreatic, ovarian, NSCLC, TNBC, mesothelioma and other MSLN-expressing cancers

MSLN EXPRESSING CANCERS



- Esophageal 35-40%
- Thymic 40-45%
- Mesothelioma 75-80%
- Breast 25-30%
- Lung 60-65%
- Biliary Tract 60-65%
- Gastric 50-55%
- Ovarian 60-65%
- Pancreatic 80-85%
- Endometrial 20-25%
- Colorectal 40-45%

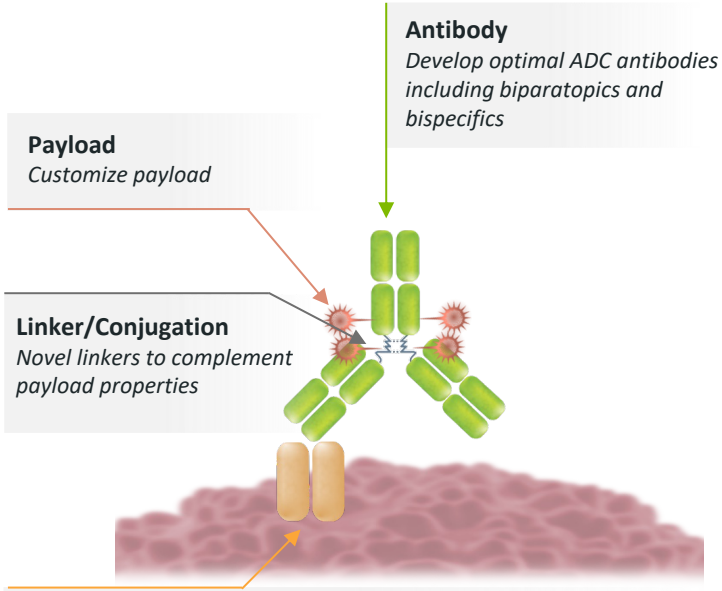
ESTIMATE OF NEWLY-DIAGNOSED MSLN+ PATIENTS IN KEY INDICATIONS



Modified from Morello et al Cancer Discovery; Vol. 6 Feb 2016 and Inaguma et al Oncotarget; Vol 8 Apr 2017

Designing Fit-for-Purpose ADC Candidates

	Zymeworks Strategy Today	Zymeworks Strategy Tomorrow
Target	Focus on targets with evidence of clinical activity in indications of unmet need	Explore novel targets
Antibody	Develop optimal ADC antibodies	Leverage bispecific and biparatopic expertise to develop optimal ADC antibodies
Linker/ Conjugation	Leverage validated peptide-cleavable linkers & stochastic conjugation	Design novel linkers to complement payload properties
Payload	Focus on novel TOPO1i ADC technology	Develop novel payloads by adapting MoAs with clinical validation to novel ADC application



ADC: antibody drug conjugate; MOA: mechanism of action

ZW191: Folate Receptor Alpha Topoisomerase-1 Inhibitor ADC

Lead Preclinical Product Candidate

Target

Folate receptor alpha (FRα, FOLR1) is a clinically validated ADC target

FRα is over-expressed on the cell surface of ovarian cancer, other gynecological cancers, and additional high incidence solid tumors with unmet medical need (NSCLC, TNBC, etc.)

Antibody

Internally discovered, novel IgG1 monospecific antibody

Optimal internalization, payload delivery and tumor penetration

Drug Linker

Cysteine conjugated, DAR8, protease cleavable, traceless drug-linker

Novel bystander-active topoisomerase-1 inhibitor

Status

MTD ≥ 30 mg/kg in two dose non-human primate (NHP) toxicology study, with favorable PK

Strong anti-tumor activity in models with a range of expression

ADC: antibody-drug conjugate; DAR: drug-to-antibody ratio; NSCLC: non small cell lung cancer; MTD: maximum tolerable dose; TNBC: triple negative breast cancer

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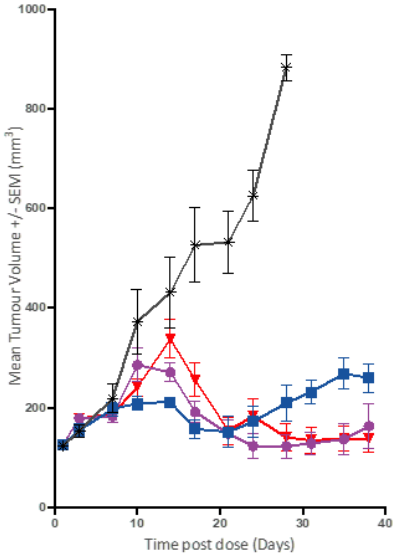
ZW191 Demonstrates Strong Anti-Tumor Activity in FRα-Expressing Models

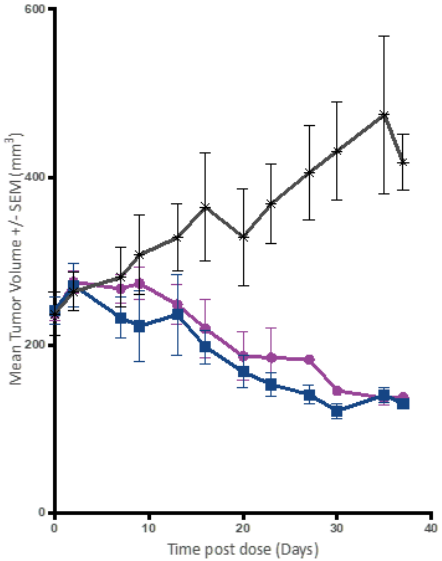
Equivalent Anti-Tumor Activity in FRα-High Expressing Xenograft Models

OV90 Ovarian Carcinoma CDX



ADCs dosed at 6 mg/kg

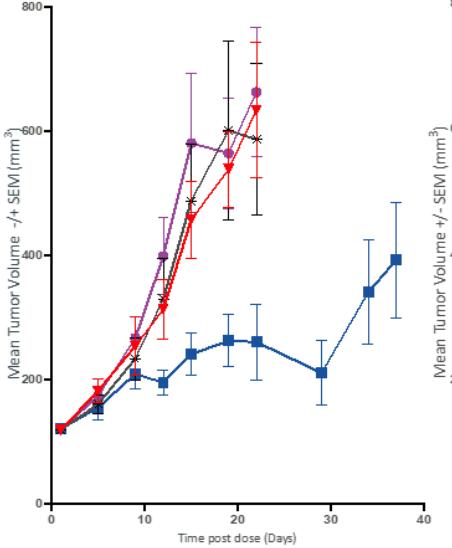
CTG-2025 Ovarian Cancer PDX



ADCs dosed at 6 mg/kg

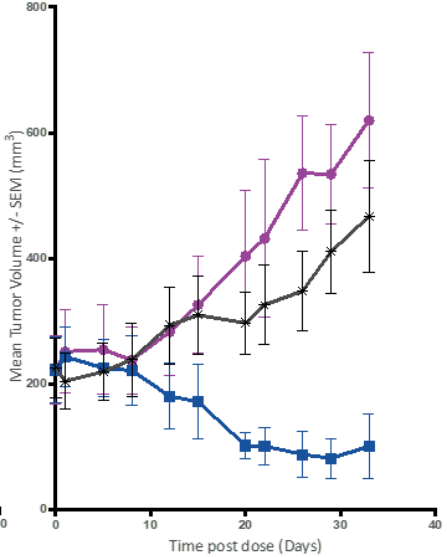
Superior Anti-Tumor Activity in FRα-Mid Expressing Xenograft Models

OVCAR-3 Ovarian Cancer CDX



ADCs dosed at 0.75 mg/kg

CTG-0958 Ovarian Cancer PDX



ADCs dosed at 6 mg/kg

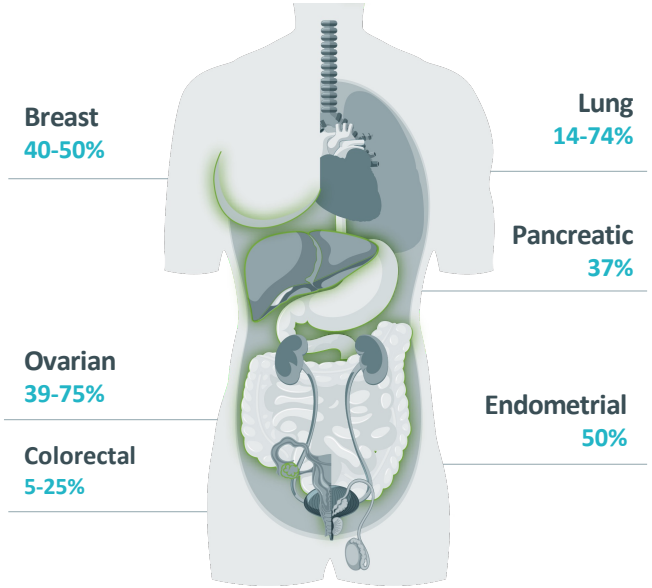
Vehicle ZW191 MORAb-202 Mirvetuximab Soravtansine

ADCs: antibody drug conjugates; CDX: cell line-derived xenograft; FRα: folate receptor alpha; PDX patient-derived xenograft

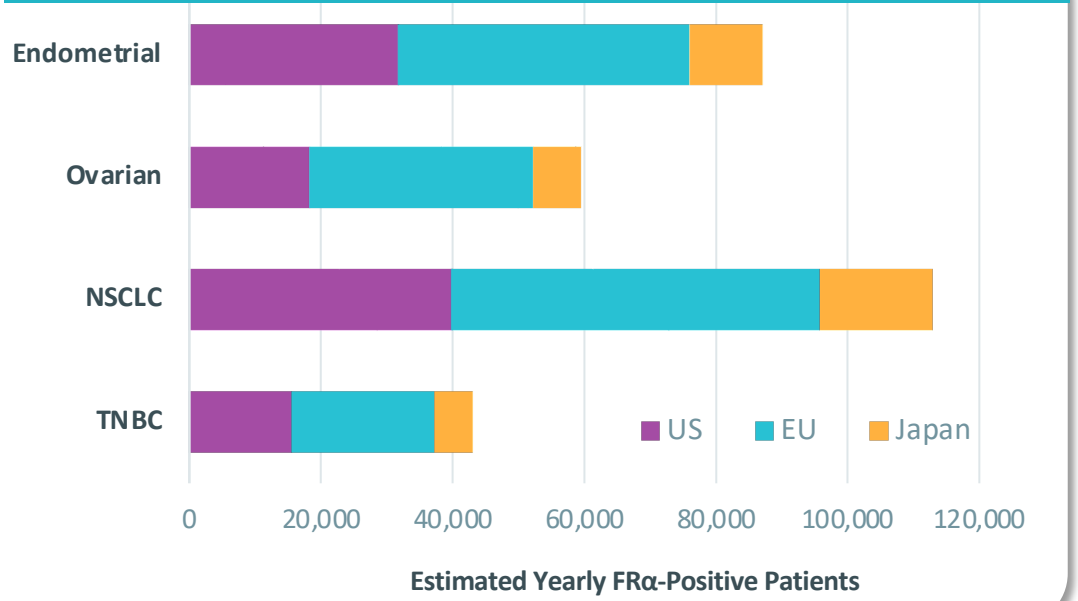
ZW191 Treatment Opportunity

- Potential best-in-class opportunity in FRα-high ovarian cancer
- Potential first- and best-in-class in FRα-high endometrial, NSCLC, TNBC, and FRα-mid/low solid tumors

FOLATE RECEPTOR ALPHA EXPRESSING CANCERS

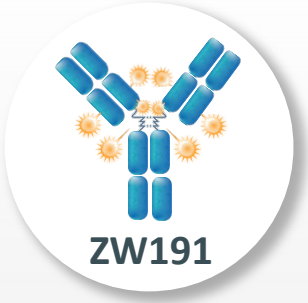


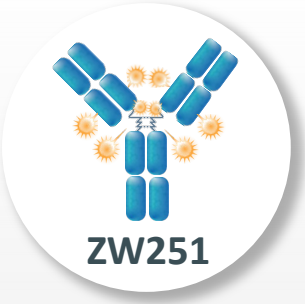
ESTIMATE OF NEWLY-DIAGNOSED FRα+ PATIENTS IN KEY INDICATIONS



Expression levels cited from multiple sources including: Senol S et al 2015; Ayada et al. Med Mol Morphol 2018; Oza AM SGO 2021; O'Shannessy DJ et al Oncotarget 2012; Nunez MI et al 2012; D'Angelica et al. Mod Path 2011; Nature Review: Clinical Oncology; Vol. 17 June 2020.
FRα: folate receptor alpha; NSCLC: non-small cell lung cancer; TNBC: triple negative breast cancer

Zymeworks' Preclinical Assets Show Significant Near-Term Potential





Target	**MSLN x CD3**	**FRα**	**GPC3**	**NaPi2b**
Format/ Technology	2 x 1 multispecific/ Azymetric™ heterodimeric Fc	Monospecific/TOPO1i ADC	Monospecific/TOPO1i ADC	Monospecific/TOPO1i ADC
Potential Indications	Ovarian cancer, pancreatic cancer, colorectal cancer	Ovarian cancer, other gynecological cancers, and other solid tumors	Liver cancer	Ovarian cancer, NSCLC
Stage	IND-Enabling	IND-Enabling	Late Discovery	Late Discovery
Next Milestone	**IND 2024**	**IND 2024**	Pilot NHP toxicology study initiated DAR optimization underway	Pilot NHP toxicology study initiated DAR optimization underway

ADC, antibody-drug conjugate; DAR, drug to antibody ratio; Fc: fragment crystallizable region of antibody; NSCLC non-small cell lung cancer; NHP, non-human primate

Zymeworks Moving Forward “5 by 5”

2017-2022

- Select Product Pipeline ✓
- Platform Technologies & Tools ✓

2022-2027

- **Accelerate Product Pipeline**
- **5 New Molecules in Clinic in 5 Years**
- **Select Product Partnerships**

5 new Zymeworks developed programs in clinic in 5 years

Key Strategic Priorities for 2022 and 2023

KEY STRATEGIC PRIORITIES	STATUS / TARGET
Financial	
Reduction in workforce	✓
Improve financial position	✓
Monetize existing financial and preclinical assets	Ongoing
Clinical	
Fully recruit HERIZON-BTC-01 pivotal trial	✓
Fully recruit HERIZON-GEA-01 pivotal trial	YE 2023
Complete/close out early-stage clinical studies	Ongoing
Release data and communicate development path for ZW49	✓
Preclinical and Platforms	
Update on progress of early-stage R&D programs	✓
Advance two new product candidates to IND stage	IND by YE 2024
Partnerships & Collaborations	
Global Zanidatamab licensing agreement (ex APAC)	✓
Continued execution on new partnerships and collaborations	Ongoing

- Priority is to **reset** and **focus** the company on maximizing shareholder value and optimizing patient outcomes
- **Identify** future development paths for zanidatamab zovodotin (ZW49), ZW171, and ZW191
- **Aggressively pursue** and **drive value** through partnerships and collaborations
- **Continually improve financial position** through non-dilutive funding sources and partnerships

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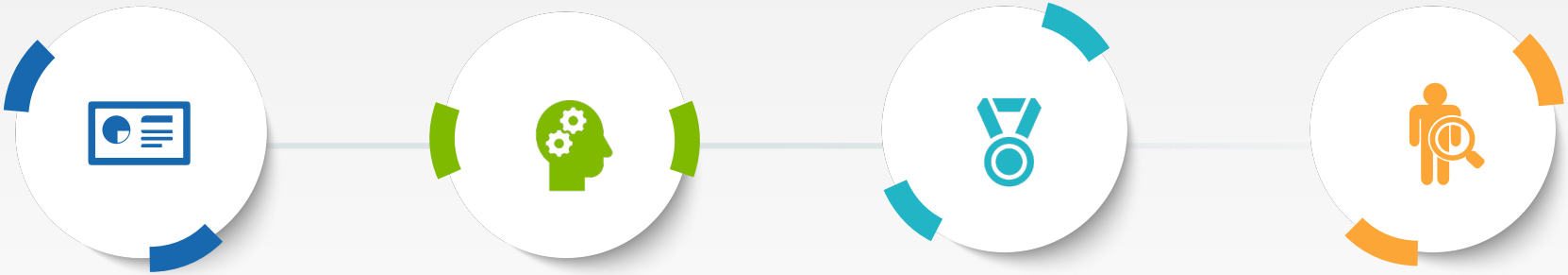
Key Expected Events & Milestones Throughout the Product Pipeline



4Q 2022

- **Early R&D Day** (October 20th)
- Late-Line **HR+ / HER2+ mBC** for zanidatamab
- **Recommended Phase 2 Dose** for zanidatamab zovodotin
- **HERIZON-BTC-01** Top-Line Data
- Expected close of JAZZ licensing agreement

1H 2023

- **HERIZON-BTC-01** Study Completion
- **Phase 2 1L GEA** Follow-Up (zanidatamab + chemotherapy)
- **Additional publications** on preclinical development candidates

2H 2023

- **HERIZON-GEA-01** Complete Patient Enrollment
- **Nomination** of next product candidate for Preclinical Development (PCD)

2024

- **Submit 2 IND Applications** for ZW171 and ZW191
- **HERIZON-GEA-01** Expect Top-Line Data
- **Continue leveraging platforms** to generate preclinical product candidates and partnerships

HR+: Hormone receptor positive; IND: investigational new drug; OS: overall survival; PFS: progression-free survival

Near-term market opportunity

with zanidatamab in GEA and BTC supported by licensing agreements with Jazz and BeiGene

Future product pipeline

driven by expected progress of ZW49, ZW171, ZW191 and next-generation ADC and multispecific platforms

Focused R&D Strategy

Drives the next wave of potential best-in-class antibody-based multifunctional therapeutics

Key Investment Highlights

Strategic priorities underpinned by renewed **management** team, **improved financial position** with **cash runway through at least 2026,** and **portfolio of existing partnership and collaborations**

Improved financial position provides ability to **rapidly advance product candidates** with a focus on next-generation **ADC and multispecific platforms**

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

Experienced and Accomplished Leadership Team

Ken Galbraith
Chair & Chief Executive Officer

Neil Klompas, CPA, CA
Chief Operating Officer

Neil Josephson, M.D.
Chief Medical Officer

Paul Moore Ph.D.
Chief Scientific Officer

Chris Astle, Ph.D.
Senior VP
and Chief Financial Officer

Mark Hollywood
Senior VP, Technical
and Manufacturing Operations

Kaycia Wilde, Ph.D.
VP, Clinical Operations

John Fann, Ph.D.
VP, Technical Operations
and Process Science

Milan Mangeshkar, Ph.D.
VP, Biometrics

Daniel Dex, JD
VP, Legal and Corporate Secretary

Jennifer Kaufman-Shaw, JD
VP, Intellectual Property

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Appendix

Zymeworks' Technologies Enable Fit-For-Purpose Design of Multispecifics

TECHNOLOGY	FEATURES	HIGHLIGHTS
Azymetric™ HetFc and HetFab heterodimeric IgG	• Industry-leading heterodimeric IgG solution • Enabling technology for bispecific and multispecific therapeutics • Superior stability, purity and modularity of Azymetric™ allows HTP screening and development of multispecifics	• Clinically validated technology • Multiple pharma partners employing
Biparatopic mAbs	• Enhanced receptor cross-linking via binding of independent epitopes	• Zanidatamab, ZW49
T Cell Engagers (TCE)	• 1+1 T cell engager applications • 2+1 T cell engager engineered to maximize therapeutic window	• JNJ-78306358; JNJ-78278343 (Phase 1) • ZW171 (2024 IND)

TriTCEs
Next Gen trispecific T cell engagers
	• Novel next gen trispecific designed to overcome TCE limitations
	  • TriTCE-costim with potential to re-invigorate 'cold' tumors
	  • TriTCE-CPI (checkpoint inhibition) to overcome suppressive tumor micro-environment
		• Candidate selection ongoing

ProTECT™ Tumor-specific immune stimulation	• Tumor-specific activity via conditional blocking to reduce off-tumor toxicities • Functional block adds checkpoint modulation to enhance efficacy	• Widens scope of possible tumor targets • Interfaces with TriTCE, Antibody or ADC
Cytokine Fc-fusions Tumor-specific cytokine activation	• Novel cytokine engineering approach combining reduced potency and tumor specificity • Can be combined or integrated with other Zymeworks molecules	• Non-core asset: Tumor restricted IL-12 (AACR 2021)

CPI, checkpoint inhibition; HTP, high-throughput screening; MTD, maximum tolerated dose;

Zymeworks' Technologies Enable Fit-For-Purpose Design of ADCs

TECHNOLOGY	FEATURES	HIGHLIGHTS
ZymeLink™ Auristatin Auristatin Drug-linker	• Potent, bystander inactive; induce markers of immunogenic cell death • N-acylsulfonamide spacer links auristatin core to stable cleavable linker; compatible with multiple conjugation strategies • IgG1-like PK and exposure	Used in: • Zanidatamab Zovodotin (ZW49) • XB002 (formerly ICON-2) • ATRC-301
ZymeLink™ Hemiasterlin Hemiasterlin Drug-linker	• Potent, bystander active • N-acylsulfonamide spacer links hemiasterlin core to stable, cleavable linker compatible with multiple conjugation strategies • IgG1-like PK and exposure	• MTD ≥ 15 mg/kg in non-human primates • DAR4 ADC at 15 mg/kg in non-human primates- no evidence of neutropenia or elevations in transaminases
TOPO1i Technology Camptothecin Drug-Linker	• Novel camptothecin payload, bystander active • Stable, cleavable linker compatible with cysteine conjugation • Anti-tumor activity across multiple programs in diverse xenograft models • IgG1-like PK and exposure	• MTD ≥ 30 mg/kg in non-human primates Used in pipeline programs: • ZW191 • ZW220 • ZW251
Site Specific Conjugation Cysteine-Insertion Technology	• Homogeneous conjugation at multiple sites • Combines with Azymetric™, multivalent linkers for precise control of DAR • Sites can mask payload hydrophobicity, protect against metabolism, and limit deconjugation	Used in non-core asset: • cMet-ZLA ADC
TLR7 ISAC Technology Immunostimulatory Drug Conjugate	• Purine-based scaffold using a peptide cleavable linker	• The Society for Immunotherapy of Cancer (SITC) 2022 abstract accepted

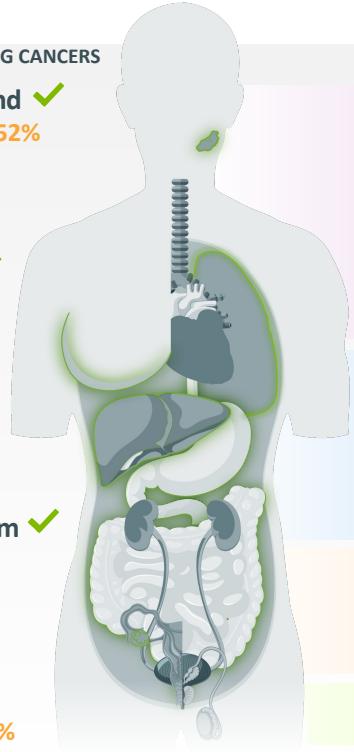
DAR, drug to antibody ratio; MTD, maximum tolerated dose

Broad Opportunities for Zanidatamab in HER2-Targeted Therapy

Advancing Zanidatamab in Two Pivotal Trials with Broad Opportunity for Additional Indications

HER2 EXPRESSING CANCERS

- **Salivary Gland** ✓ — 17-44% | 12-52%
- **Lung** ✓ — 2.5% | 2-3%
- **Pancreas** ✓ — 26% | 2%
- **Bladder** — 12.4% | 9%
- **Ovarian** ✓ — 27% | 7%
- **Endometrium** ✓ — 18-80% | 4%
- **Prostate** — 10% | 6%
- **Cervix** — 21% | 0.5-14%



	PHASE 1	PHASE 2	PIVOTAL
Breast ✓ 15-20% | 20%	3L+ Zanidatamab + Ibrance (anti-CDK4/6) + Fulvestrant		
	1L Zanidatamab + Docetaxel		
	3L+ Zanidatamab + Evorpacept (CD47-blocker)		
	3L+ Zani + Chemo		
Stomach ✓ 20% | 11-16%	1L Zanidatamab + SOC Chemo ± Tislelizumab *vs* Herceptin + SOC Chemo		HERIZON
	1L Zanidatamab + SOC Chemotherapy + Tislelizumab		
	1L Zanidatamab + SOC Chemotherapy		
Biliary Tract ✓ 20% | 5-15%	2L Zanidatamab Monotherapy		HERIZON
	1L Zanidatamab + SOC (cisplatin + gemcitabine)		
Colorectal ✓ 5% | 6%	1L Zanidatamab + SOC (mFOLFOX6 ± bevacizumab)		

SOC = Standard of Care

HER2 EXPRESSION | AMPLIFICATION

✓ ZANIDATAMAB SINGLE AGENT ACTIVITY

Modified from Oh D-Y & Bang Y-J 2019 Nat Rev Clin Onc

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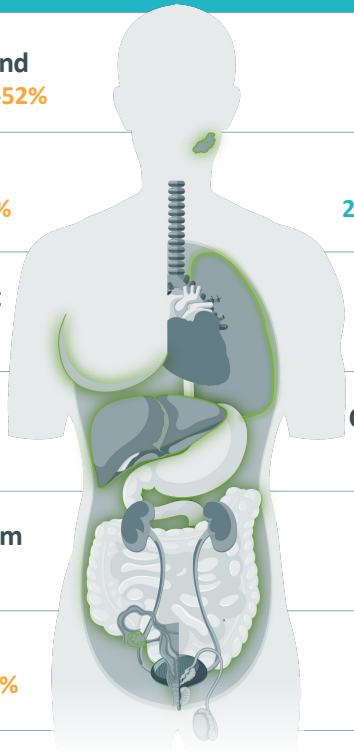
Patient Populations Support Broad Opportunities

HER2 EXPRESSION | AMPLIFICATION

Estimated HER2+ Patient Population[1]	SINGLE AGENT ACTIVITY ZANI | ZW49	HER2 EXPRESSING CANCERS	SINGLE AGENT ACTIVITY ZANI | ZW49	Estimated HER2+ Patient Population[1]
5,100 | 5,300	✓	**Salivary Gland** 17-44% | 12-52%	**Lung** 2.5% | 2-3% ✓ ✓	18,600 | 18,600
122,800 | 140,400	✓ ✓	**Breast** 15-20% | 20%	**Stomach** 20% | 11-16% ✓ ✓	52,400[2]
7,200[3]	✓ ✓	**Biliary Tract** 20% | 5-15%	**Pancreas** 26% | 2% ✓ ✓	50,400 | 3,900
37,700 | 9,800	✓ ✓	**Ovarian** 27% | 7%	**Colorectum** 5% | 6% ✓	32,000 | 38,400
160,700 | 13,100	✓ ✓	**Endometrium** 18-80% | 4%	**Bladder** 12.4% | 9% ✓ ✓	36,000 | 26,100
25,200 | 8,700		**Cervix** 21% | 0.5-14%	**Prostate** 10% | 6%	145,500 | 87,300



[1] Estimates rounded to nearest hundred patients and averaged where represented by a range of expression / amplification; represent potential HER2+ patients by indication for US, EU28, and Japan; excludes BeiGene controlled commercial territories.
[2] ToGA Trial; Yan M, et al., Cancer Metastasis Rev (2015); Meric-Bernstam et al., Clinical Cancer Research (2018); [3] Roche Diagnostics biomarker data; 5 Pillai RN et al Cancer 2017; 123:4099-4105, Arcila ME eet al Clin Cancer Res. 2012; 18: 4910-4918, Mazieres J et al J Clin Oncol. 2013; 31: 1997-2003;
HER2 expression and amplification as mod Modified from Oh D-Y & Bang Y-J 2019 Nat Rev Clin Onc; incidence rate per GLOBOCAN and bioStrategies forecast models.

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HERIZON-GEA-01: Dosing Regimens and Statistical Analysis

Dosing Regimens[1]

- Zanidatamab: Subjects <70 kg: 1,800 mg IV of each 21-day cycle; Subjects ≥70 kg: 2,400 mg IV of each 21-day cycle
- Tislelizumab: 200 mg IV on Day 1 of each 21-day cycle
- Trastuzumab (Herceptin®; active comparator): 6 mg/kg IV of Day 1 of each 21-day cycle (8 mg/kg IV loading dose on Cycle 1, Day 1)
- CAPOX (combination chemotherapy): Capecitabine 1,000 mg/m^2 PO bid (total daily dose of 2,000 mg/m^2) from the evening of Day 1 to the morning of Day 15 of each 21-day cycle plus oxaliplatin 130 mg/m^2 IV on Day 1 of each 21-day cycle.
- FP (combination chemotherapy): 5-FU 800 mg/m^2/day continuous IV infusion on Days 1 to 5 of each 21-day cycle plus cisplatin 80 mg/m^2 (60 mg/m^2 for subjects with GFR 51-61 mL/min at baseline) IV on Day 1 of each 21-day cycle

Statistical Analysis[1]

- Efficacy assessed in the intent-to-treat population, including all randomized subjects; safety assessed in all randomized subjects receiving any amount of treatment
- Comparisons of both experimental arms (2 and 3) to the control arm (1) for the primary endpoint will be performed using performed using a 2-sided, stratified, log-rank test after adjusting for the randomization stratification factors
- The overall alpha for comparisons is 0.05 (2-sided). The primary analyses of PFS or OS will be performed once the target event counts for each comparison are reached. Estimates of the hazard ratio (HR) and corresponding 95% CIs will be obtained from a Cox proportional hazards model that includes the stratification factors
- Sample size of 714 subjects is based on providing 95% power and 80% power to detect PFS HRs of 0.65 for Arm C versus Arm A and 0.73 for Arm B versus Arm A, respectively, at the time of final PFS analysis, and 80% power to detect an OS HR of 0.72 for Arm C versus Arm A at the time of final OS analysis
- An interim analysis for OS will be performed at the time of the final PFS analysis

[1] https://doi.org/10.2217/fon-2022-0595

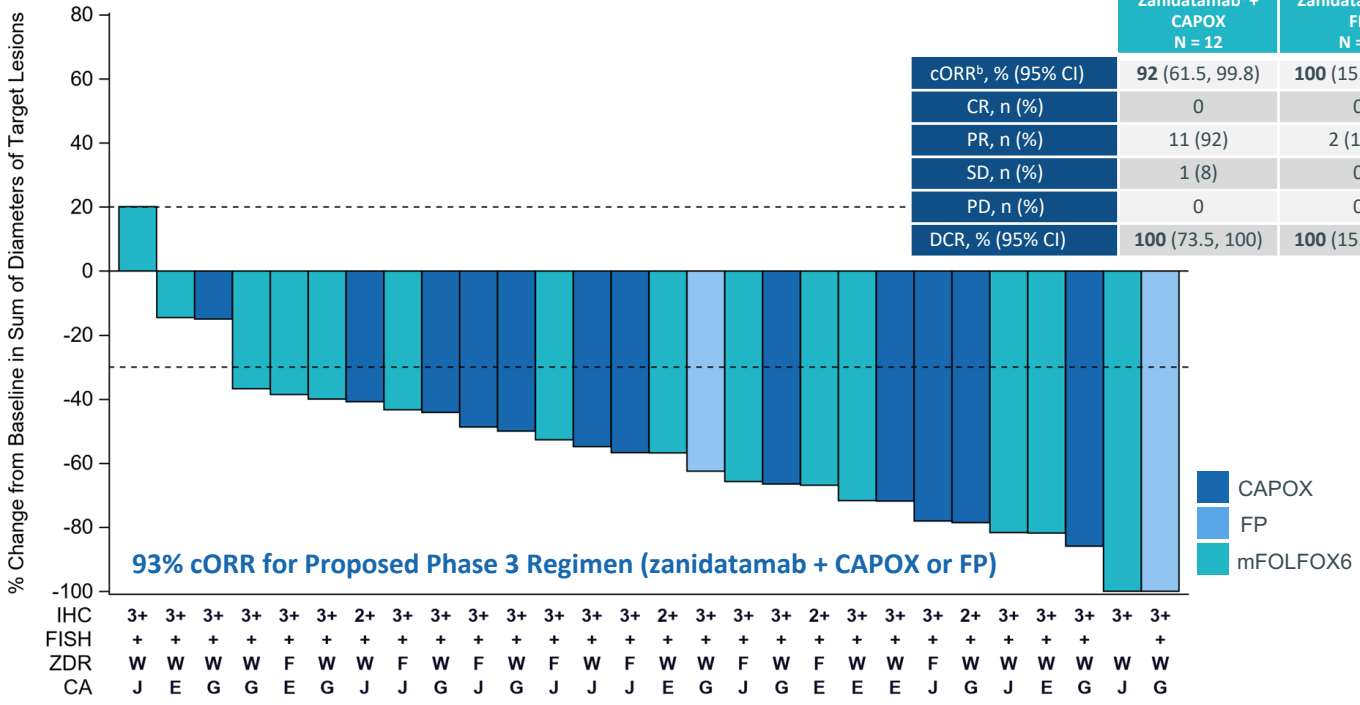
BICR: Blind independent central review; GEA: gastroesophageal adenocarcinoma; PFS: Progression-free survival; OS: overall survival

Zanidatamab Plus Chemotherapy in HER2+ First-Line GEA

As reported at ESMO | Sep 2021 (Update to be presented in 1H-2023 at a major medical meeting)

Durable Anti-Tumor Activity Observed in Majority of HER2+ GEA Patients

	Zanidatamab[a] + CAPOX N = 12	Zanidatamab[a] + FP N = 2	Zanidatamab[a] + mFOLFOX6 N = 14	Total N = 28
cORR[b], % (95% CI)	**92** (61.5, 99.8)	**100** (15.8, 100)	**57** (28.9, 82.3)	**75** (55.1, 89.3)
CR, n (%)	0	0	1 (7)	1 (4)
PR, n (%)	11 (92)	2 (100)	7 (50)	20 (71)
SD, n (%)	1 (8)	0	3 (21)	4 (14)
PD, n (%)	0	0	3 (21)	3 (11)
DCR, % (95% CI)	**100** (73.5, 100)	**100** (15.8, 100)	**79** (49.2, 95.3)	**89** (71.8, 97.7)



[a]HER2-positive was defined as IHC 3+ or IHC 2+/FISH+. [b]cORR included a baseline scan and a confirmatory scan obtained ≥ 4 weeks following initial documentation of objective response; the efficacy-evaluable population was defined as all HER2-positive subjects who had ≥ 1 evaluable post-baseline disease assessment or discontinued study treatment due to death or clinical progression.
5-FU: 5-fluorouracil; CAPOX: capecitabine plus oxaliplatin; cORR: confirmed objective response rate; CR: complete response; DCR: disease control rate; E: esophageal cancer; F: flat dosing; FISH: fluorescence in situ hybridization; FP: 5-FU and cisplatin; G: gastric cancer; IHC: immunohistochemistry; J: gastroesophageal junction cancer; mFOLFOX6: 5-FU plus oxaliplatin and leucovorin; NR: not reached; ORR: objective response rate (CR + PR); PD: progressive disease; PR: partial response; SD: stable disease; W: weight-based dosing; ZDR: zanidatamab dosing regimen.

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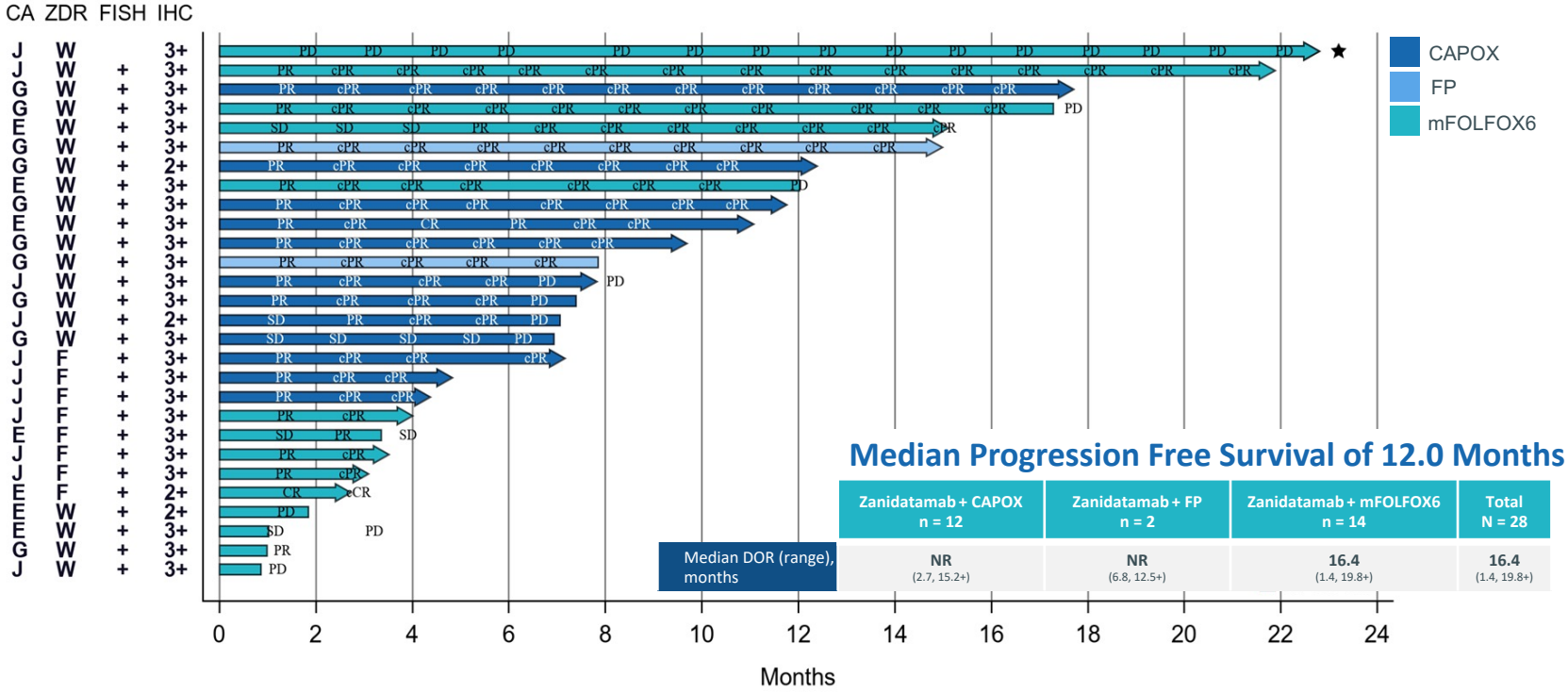
Zanidatamab Plus Chemotherapy in HER2+ First-Line GEA

As reported at ESMO | Sep 2021 (Update to be presented in 1H-2023 at a major medical meeting)

Durable Anti-Tumor Activity Observed in Majority of HER2+ GEA Patients



Median Progression Free Survival of 12.0 Months

	Zanidatamab + CAPOX n = 12	Zanidatamab + FP n = 2	Zanidatamab + mFOLFOX6 n = 14	Total N = 28
Median DOR (range), months	NR (2.7, 15.2+)	NR (6.8, 12.5+)	16.4 (1.4, 19.8+)	16.4 (1.4, 19.8+)

★ An MRI performed for neurologic symptoms on Day 8 demonstrated brain metastases, which were treated with radiation therapy. Subject remained on mFOLFOX6-1 with zanidatamab and has had long term disease control since treatment of brain metastases.

5-FU: 5-fluorouracil; CA: primary tumor location; CAPOX: capecitabine plus oxaliplatin; cCR: confirmed CR; CR: complete response; cPR: confirmed PR; DOR: duration of response; E: esophageal cancer; F: flat dosing; FISH: fluorescence in situ hybridization; FP: 5-FU plus cisplatin; G: gastric cancer; IHC: immunohistochemistry; J: gastroesophageal junction cancer; mFOLFOX6: 5-FU plus oxaliplatin and leucovorin; NR: not reached; PD: progressive disease; PR: partial response; SD: stable disease; W: weight-based dosing; ZDR: zanidatamab dosing regimen; + = indicates that the subject is in response at the time of data extraction.

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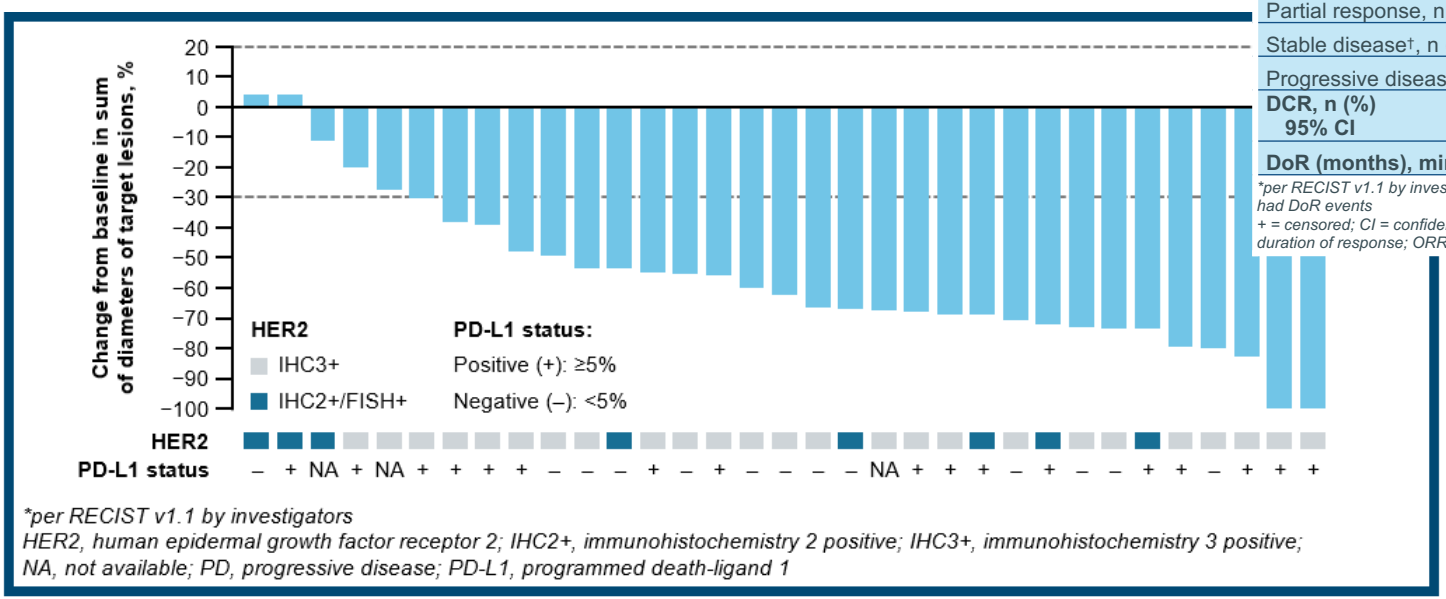
Zanidatamab Plus Tislelizumab and Chemotherapy HER2+ First-Line GEA

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022

Zanidatamab + tislelizumab + CAPOX induces deep responses in the majority of patients



*per RECIST v1.1 by investigators
HER2, human epidermal growth factor receptor 2; IHC2+, immunohistochemistry 2 positive; IHC3+, immunohistochemistry 3 positive; NA, not available; PD, progressive disease; PD-L1, programmed death-ligand 1

Table 3. Disease response*

	Total (N=33)
Confirmed ORR, n (%) **95% CI**	**25 (75.8)** 57.7, 88.9
Complete response, n (%)	1 (3.0)
Partial response, n (%)	24 (72.7)
Stable disease†, n (%)	8 (24.2)
Progressive disease, n (%)	0 (0)
DCR, n (%) **95% CI**	**33 (100.0)** 89.4, 100.0
DoR (months), min, max†	**2.1+, 18.2+**

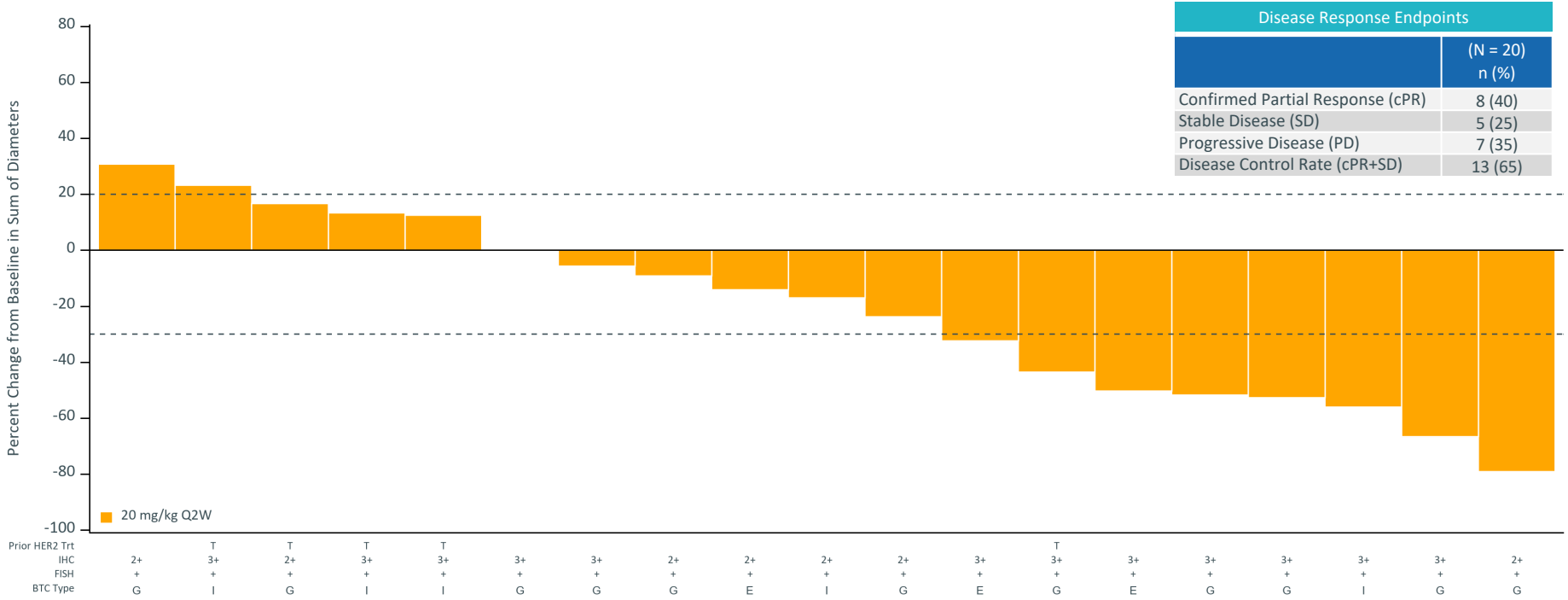
*per RECIST v1.1 by investigators; †28% of patients with a confirmed response had DoR events
+ = censored; CI = confidence interval; DCR = disease control rate; DoR = duration of response; ORR = objective response rate

Source: J Clin Oncol 40, 2022 (suppl 16; abstr 4032)

Zanidatamab Monotherapy in HER2-Expressing Late-Line BTC

As reported at ASCO GI | Jan 2021

Chemo-Free Regimen Positioning to be First HER2-Targeted Therapy Approved for Biliary Tract Cancer Patients



Disease Response Endpoints	
	(N = 20) n (%)
Confirmed Partial Response (cPR)	8 (40)
Stable Disease (SD)	5 (25)
Progressive Disease (PD)	7 (35)
Disease Control Rate (cPR+SD)	13 (65)

E: Extrahepatic Cholangiocarcinoma; FISH: fluorescence in situ hybridization; I: Intrahepatic Cholangiocarcinoma; IHC: immunohistochemistry; G: Gallbladder; T: trastuzumab; Trt: treatment.
Response-evaluable: all treated patients with measurable disease who had at least one evaluable, post-baseline disease assessment (per RECIST 1.1) or discontinued study treatment due to death or clinical progression. Note: One patient was not response evaluable because they withdrew from the study. One patient in the response-evaluable set died prior to the post-baseline tumor measurement and is not included in the plot (counted as PD). Data snapshot from unlocked database 16 November 2020 and subject to change.

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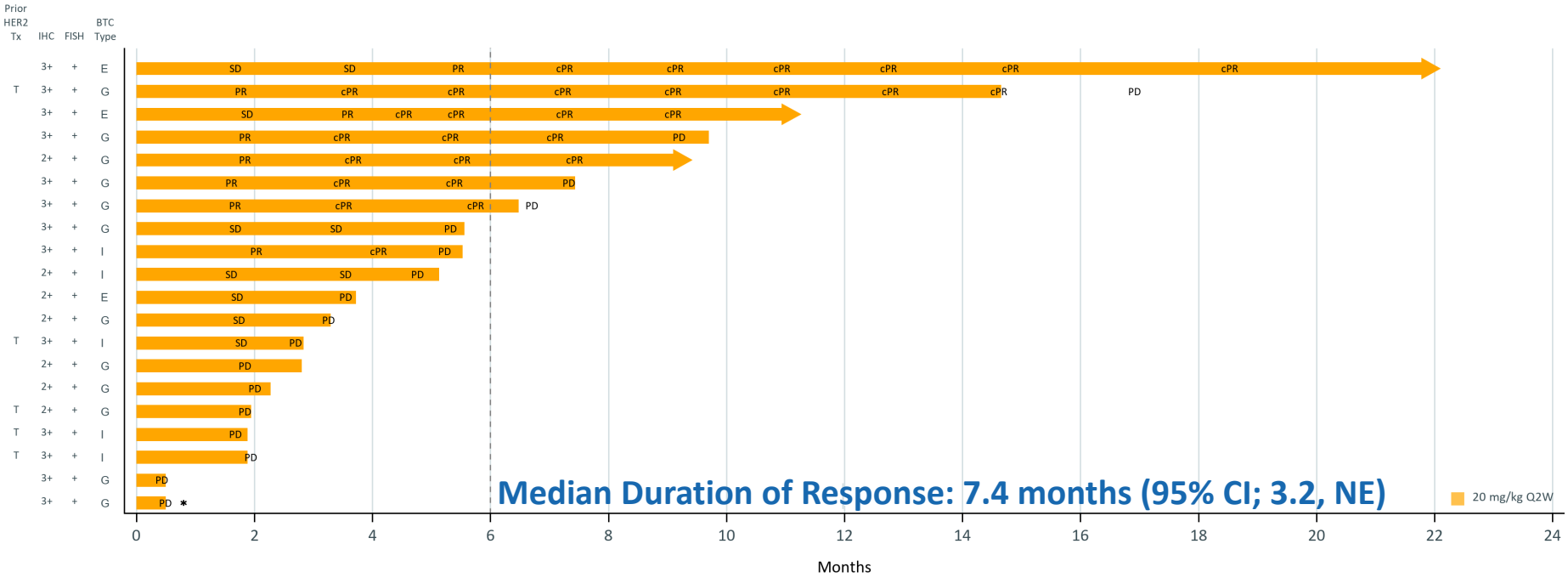
Zanidatamab Monotherapy in HER2-Expressing Late-Line BTC

As reported at ASCO GI | Jan 2021

Data Supports Pivotal Trial in Second-Line Biliary Tract Cancers

(HERIZON-BTC-01; NCT04466891; Enrollment completed April 2022)



(c)PR: (confirmed) partial response; E: extrahepatic cholangiocarcinoma, FISH: fluorescence in situ hybridization; I: intrahepatic cholangiocarcinoma, IHC: immunohistochemistry; G: gallbladder; PR: partial response; PD: progressive disease; SD: stable disease; T: trastuzumab; Tx: Treatment. *, death. Data snapshot from unlocked database 16 November 2020 and subject to change.

Zanidatamab in Combination with Docetaxel for First-Line Treatment of Breast Cancer

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022

Promising Efficacy in First-Line Breast Cancer

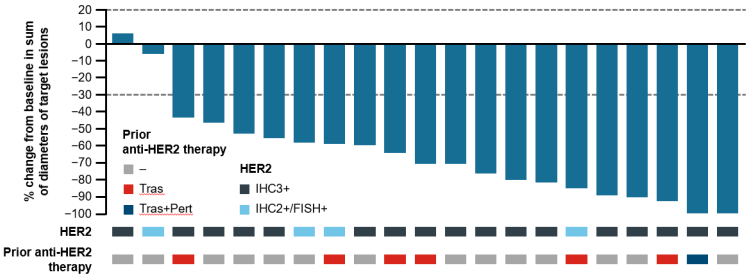
- Of the 21 efficacy evaluable patients, the confirmed objective response rate (ORR) was 90.5% (95% CI: 69.6, 98.8) (Table 3) with 15 patients (78.9%) who were ongoing responders.
- The disease control rate was 95.2% (95% CI: 76.2, 99.9) (Table 3); 20 patients had controlled disease
- The 6-month progression-free survival rate was 95.2% (95% CI: 70.7, 99.3)
- Study fully enrolled 1Q22 with ~35 patients

Table 3. Disease response*

	Total (N=21)
cORR†, %	**90.5**
95% CI	69.6, 98.8
Complete response, n (%)	1 (4.8)
Partial response, n (%)	18 (85.7)
Stable disease, n (%)	1 (4.8)
Progressive disease, n (%)	1 (4.8)
DCR†, %	**95.2**
95% CI	76.2, 99.9
DoR (months), min, max‡	**1.4+, 12.4**

**In the efficacy evaluable analysis set; †per RECIST v1.1 by investigators; ‡15.8% of patients had DoR events +, censored; CI, confidence interval; cORR, confirmed objective response rate; DCR, disease control rate; DoR, duration of response*

Figure 2. Best change in target lesion*



**per RECIST v1.1 by investigator in the efficacy evaluable analysis set which was defined as patients with at least one dose and at least one post-baseline tumor assessment FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor 2; IHC2+, immunohistochemistry 2 positive; IHC3+, immunohistochemistry 3 positive; INV, investigator; Pert, pertuzumab; Tras, trastuzumab*

Zanidatamab Zovodotin Monotherapy in HER2+ Cancers

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022

Baseline Characteristics	DE (n=52)	DX (n=25)	Total (N = 77)
Median age (range), years	58.5 (24 – 83)	59 (32 – 75)	59 (24 – 83)
Female, n (%)	32 (62)	13 (52)	45 (58)
Race, n (%)			
White	33 (63)	11 (44)	44 (57)
Asian	11 (21)	12 (48)	23 (30)
Other*	8 (15)	2 (8)	10 (13)
ECOG PS 1, n (%)	36 (69)	15 (60)	51 (66)
Primary diagnosis, n (%)			
GEA	13 (25)	8 (32)	21 (27)
Breast Cancer	10 (19)	7 (28)	17 (22)
All other	29 (56)	10 (40)	39 (51)
HER2 Status, n (%)**			
IHC3+	26 (50)	19 (76)	45 (58)
IHC2+/FISH+	6 (12)	6 (24)	12 (16)
Patients with prior HER2-targeted therapies, n (%)	37 (71)	16 (64)	53 (69)
Median prior systemic regimens in metastatic setting, n (range)	3 (1 – 16)	3 (1 – 13)	3 (1 – 16)

Data cutoff: 09 Jun 2022

*Other included: Black or African American and Not Reported/Unknown/Multiple.
**HER2 status for the remaining 20 patients included: ERBB2 Gene Amp. = 17 (22%) and FISH amp. = 3 (4%)
DE = dose escalation; DX = dose expansion; ECOG PS = Eastern Cooperative Oncology Group performance status; FISH = fluorescence *in situ* hybridization; GEA = gastroesophageal adenocarcinoma; IHC = immunohistochemistry

- As of 09 Jun 2022, a total of 77 patients were treated across DE (all patients) and DX (2.5 mg/kg Q3W) parts of the study
  - 9 (12%) continue ZW49 treatment

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Zanidatamab Zovodotin Monotherapy in HER2+ Cancers- TRAEs

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022

Preferred Term	Dose Escalation (DE)										Dose Expansion (DX)	DE+DX	DE+DX
	1 mg/kg QW* (n=4)	1.25 mg/kg QW (n=4)	1.5 mg/kg QW (n=6)	1.75 mg/kg QW** (n=7)	1 mg/kg Q2W* (n=6)	2 mg/kg Q2W* (n=8)	2 mg/kg Q3W (n=6)	2.5 mg/kg Q3W (n=5)	3 mg/kg Q3W (n=6)	Total (n=52)	2.5 mg/kg Q3W (n=25)	2.5 mg/kg Q3W (n=30)	Total (N=77)
TRAE of any Grade in ≥ 20% patients, n (%)													
Any AE	4 (100)	4 (100)	6 (100)	6 (86)	5 (83)	7 (88)	5 (83)	5 (100)	6 (100)	48 (92)	22 (88)	27 (90)	70 (91)
Keratitis	2 (50)	2 (50)	3 (50)	3 (43)	0	4 (50)	2 (33)	3 (60)	4 (67)	23 (44)	10 (40)	13 (43)	33 (43)
Alopecia	2 (50)	1 (25)	4 (67)	0	1 (17)	4 (50)	1 (17)	0	1 (17)	14 (27)	5 (20)	5 (17)	19 (25)
Diarrhoea	3 (75)	0	2 (33)	1 (14)	0	2 (25)	1 (17)	2 (40)	1 (17)	12 (23)	7 (28)	9 (30)	19 (25)
≥ Grade 3 TRAE in ≥ 1 patient, n (%)													
Any AE	0	1 (25)	0	1 (14)	0	2 (25)	0	0	0	4 (8)	5 (20)	5 (17)	9 (12)
Keratitis	0	0	0	1 (14)	0	1 (12)	0	0	0	2 (4)	1 (4)	1 (3)	3 (4)
TR SAEs of any Grade in ≥ 1 patient, n (%)													
Any SAE	0	0	0	0	0	0	1 (17)	0	0	1 (2)	2 (8)	2 (7)	3 (4)
IRR	0	0	0	0	0	0	1 (17)	0	0	1 (2)	1 (4)	1 (3)	2 (3)
ECG QT Prolonged	0	0	0	0	0	0	0	0	0	0	1 (4)	1 (3)	1 (1)

Data cutoff: 09 Jun 2022

* Includes patients enrolled prior to mandatory ocular prophylaxis.
**One additional patient was enrolled in this cohort to account for a non-DLT evaluable patient.
AE = adverse event; DLT = dose-limiting toxicity; ECG = electrocardiogram; IRR = infusion-related reaction; QT = QT interval; QW = once every week; Q2W = once every 2 weeks; Q3W = once every 3 weeks; TRAE = treatment-related adverse event; SAE = serious adverse event

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Zanidatamab Zovodotin Monotherapy in HER2+ Cancers- Safety Summary

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022

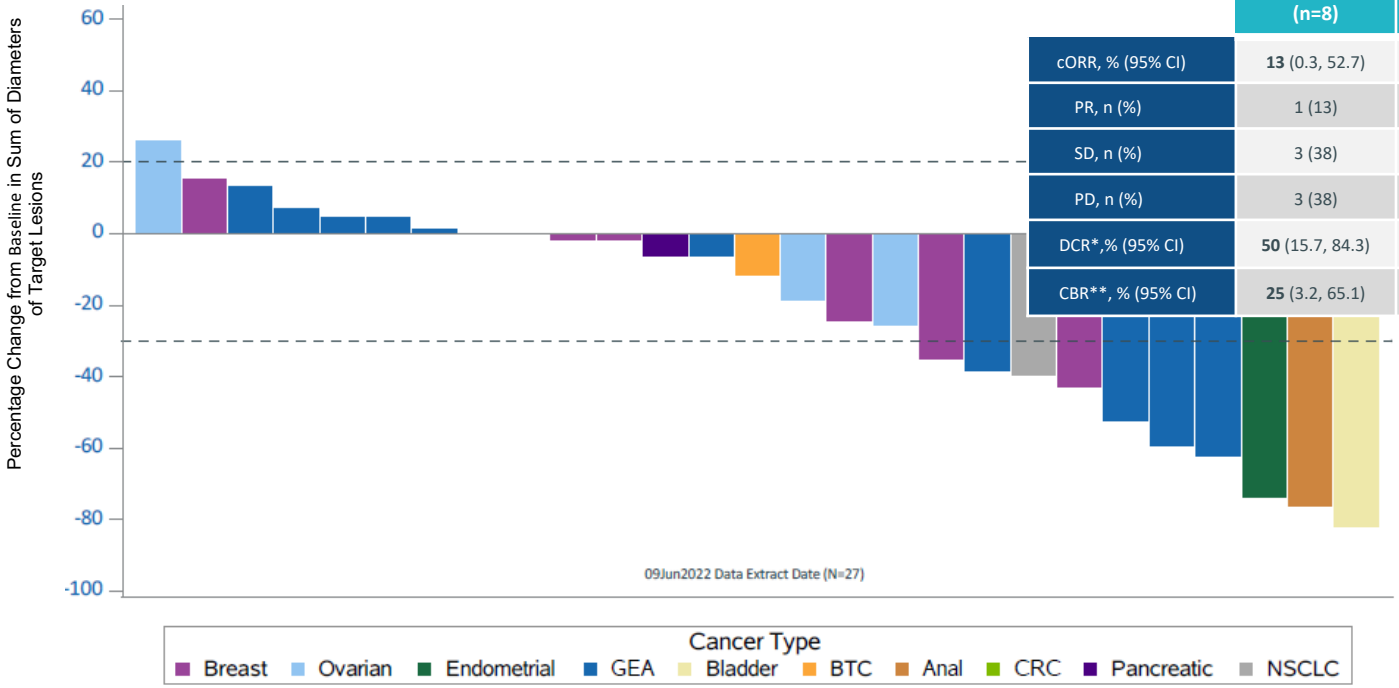
- The MTD has not been reached
- Two dose-limiting toxicities (Grade 2 keratitis > 14 days) were observed in 1 patient each at the 1.75 mg/kg QW (DE) and 2.5 mg/kg Q3W (DX) cohorts
- No interstitial lung disease (ILD) or pneumonitis were reported
- There were no treatment-related deaths
- Treatment-related keratitis was reported in 33 (43%) patients. All keratitis events decreased to Grade 1 or resolved.
    - Mandatory ocular prophylaxis:
        - Prednisolone, tetrahydrozoline (0.05%) or naphazoline (0.012%) or equivalent, and cooling masks
- Dose reduction was required in 16 (21%) patients due to treatment-related AEs* (10 [19%] patients in DE and 6 [24%] patients in DX). These patients continued receiving ZW49 at a reduced dose level.

*12 patients had keratitis (including 2 patients who also reported dry eye) and 1 patient each had an event of infusion-related reaction, punctuate keratitis, prolonged ECG QT, and neutrophil decreased.
AE = adverse event; DE= dose escalation; DX = dose expansion; ECG = electrocardiogram; MTD = maximum tolerated dose; Q3W = once every 3 weeks; QT = QT interval

Zanidatamab Zovodotin Monotherapy in HER2+ Cancers

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022

Zanidatamab Zovodotin Shows Promising Single-Agent Activity in a Variety of Tumor Types at 2.5 mg/kg Q3W



	Breast (n=8)	GEA (n=11)	All Other (n=10)	Total (N=29)#
cORR, % (95% CI)	**13** (0.3, 52.7)	**36** (10.9, 69.2)	**40** (12.2, 73.8)	**31** (15.3, 50.8)
PR, n (%)	1 (13)	4 (36)	4 (40)	9 (31)
SD, n (%)	3 (38)	4 (36)	5 (50)	12 (41)
PD, n (%)	3 (38)	3 (27)	1 (10)	7 (24)
DCR*,% (95% CI)	**50** (15.7, 84.3)	**73** (39.0, 94.0)	**90** (55.5, 99.7)	**72** (52.8, 87.3)
CBR**, % (95% CI)	**25** (3.2, 65.1)	**36** (10.9, 69.2)	**50** (18.7, 81.3)	**38** (20.7, 57.7)

Note: One patient each with breast cancer and GEA who had no post-baseline assessments were excluded from the plot

#One patient of the 30 treated at 2.5 mg/kg Q3W was HER2 negative per central review and not included. *DCR = CR, PR, or SD. **CBR = SD ≥ 24 weeks or best overall response of CR or PR.

BTC = biliary tract cancer; CBR = clinical benefit rate; cORR = conxfirmed objective response rate; CRC = colorectal cancer; DCR = disease control rate; DE = dose escalation; DX = dose expansion; GEA = gastroesophageal adenocarcinoma; NSCLC = non-small cell lung cancer; PD = progressive disease; PR = partial response; Q3W = once every 3 weeks; SD = stable disease

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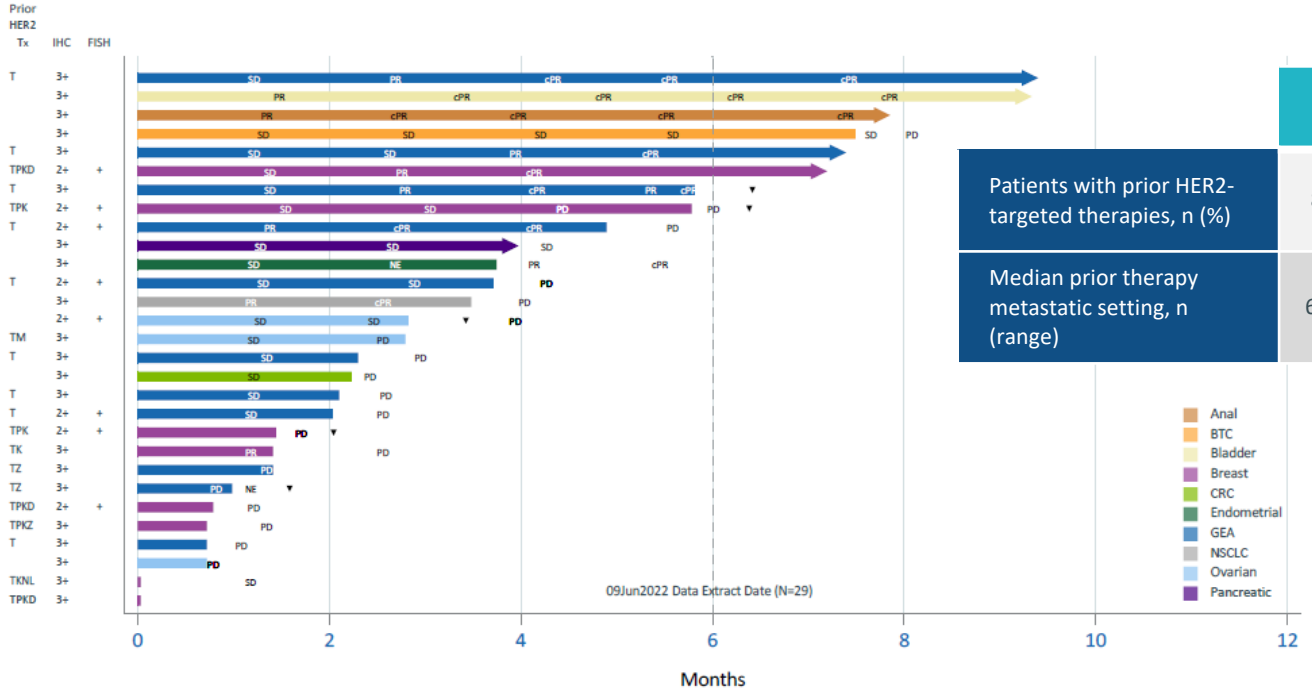
Zanidatamab Zovodotin Monotherapy in HER2+ Cancers

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022

Durable Responses Seen in a Heavily Pretreated Patient Population



	Breast (n=8)	GEA (n=11)	Other (n=10)	Total (N=29)[#]
Patients with prior HER2-targeted therapies, n (%)	8 (100)	11 (100)	1 (10)	20 (69)
Median prior therapy metastatic setting, n (range)	6 (3, 13)	4 (1, 8)	2 (1, 6)	3 (1, 13)

[#]One patient of the 30 treated at 2.5 mg/kg Q3W was HER2 negative per central review and not included.

BTC = biliary tract cancer; cPR = confirmed partial response; CRC = colorectal cancer; D = T-DXd; DE = dose escalation; DX = dose expansion; FISH = fluorescence *in situ* hybridization; GEA = gastroesophageal adenocarcinoma;
IHC = immunohistochemistry; K = T-DM1; L = lapatinib; M = margetuximab; N = neratinib; NE = not evaluable; NSCLC = non-small cell lung cancer; P = pertuzumab; PD = progressive disease;
PR = partial response; Q3W = once every 3 weeks; SD = stable disease; T = trastuzumab; Tx = therapy; U = tucatinib; Z = zanidatamab