



# Jefferies Healthcare Conference

**Ken Galbraith, Chair & CEO**

June 8, 2022

**NYSE: ZYME**

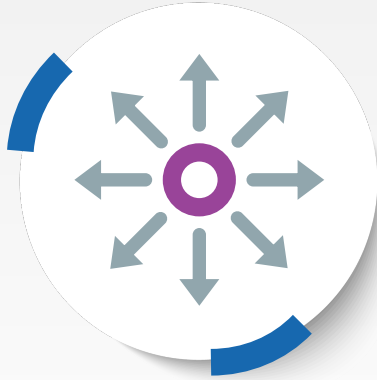
[www.zymeworks.com](http://www.zymeworks.com)

# Forward-Looking Statements

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 include statements that may relate to our plans, objectives, goals, strategies, future events, future revenue or performance, capital expenditures, financing needs and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as “subject to,” “believe,” “anticipate,” “plan,” “expect,” “intend,” “estimate,” “project,” “may,” “will,” “should,” “would,” “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, our examination of historical operating trends, are based upon our current expectations and various assumptions. We may not realize our expectations, and our beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of risks and uncertainties, including those described in the "Risk Factors" 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.

# 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



## Zymeworks is Leading the Wave of Multifunctional Drug Development

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

# Novel Platforms Enable Unique and Differentiated Multifunctional Therapeutics

## Our Approach to Platform Development:

### Azymetric™



#### Bispecific Antibody Platform

- Dual targeting of receptors and ligands
- IgG1-like biophysical and functional properties
- IgG1-like manufacturing and purification protocols

### Drug Conjugate Platforms



#### Fit-For Purpose ADC Candidate Creation

- ZymeLink™ Auristatin
- ZymeLink™ Hemiasterlin
- TOPO1i Platform
- Cysteine-Insertion Conjugation Platform

### EFFECT™



#### Immune Function Modulating Platform

- 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



# Integrated Drug Conjugate Platforms

## Our Four Core Technologies Allow for Fit-For-Purpose Design of ADC Candidates and Complement Existing Technology Platforms

### ZymeLink™ Auristatin

#### Proprietary Auristatin Drug-linker

- Clinical application (ZW49, XB002) and out-licensing (ATRC-301)
- Potent, bystander inactive ADCs induce markers of immunogenic cell death
- Stable, cleavable linkers compatible with multiple conjugation strategies
- Anti-tumor activity across multiple different targets
- IgG1-like PK and exposure
- Robust manufacturing process in place

### ZymeLink™ Hemiasterlin

#### Proprietary Hemiasterlin Drug-linker

- Potent, bystander active ADCs
- Stable, cleavable linkers compatible with multiple conjugation strategies
- Demonstrated preclinical efficacy across multiple programs
- IgG1-like PK and exposure
- DAR4 ADC is tolerated at 15 mg/kg in non-human primates with no evidence of neutropenia or elevations in transaminases
- Scalable synthetic process

### TOPO1i Platform

#### Proprietary Camptothecin Drug-Linker

- Potent, bystander-active ADCs
- Stable, cleavable linker compatible with cysteine conjugation
- Anti-tumor activity across multiple programs in diverse preclinical xenograft models
- IgG1-like PK and exposure
- Excellent tolerability profile in preclinical studies suggests favorable therapeutic index

### Site-Specific Conjugation

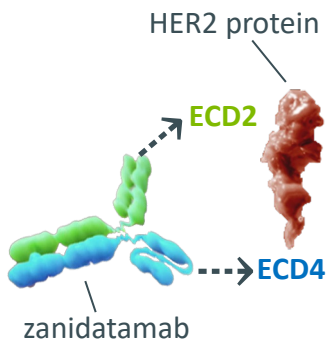
#### Proprietary Cysteine-Insertion Conjugation Platform

- Enables homogeneous conjugation at multiple sites
- Sites can mask payload hydrophobicity, protect against metabolism, and limit deconjugation
- Combining cysteine-insertion conjugation platform with Azymetric™ platform and multivalent drug linkers enables precise control of DAR

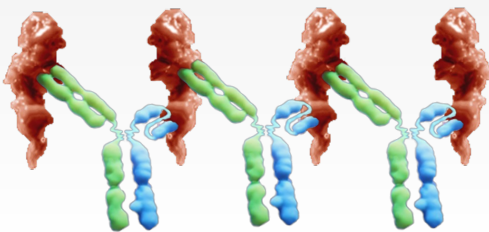
# Zanidatamab: A Biparatopic Bispecific Antibody for HER2-Expressing Cancers

## 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

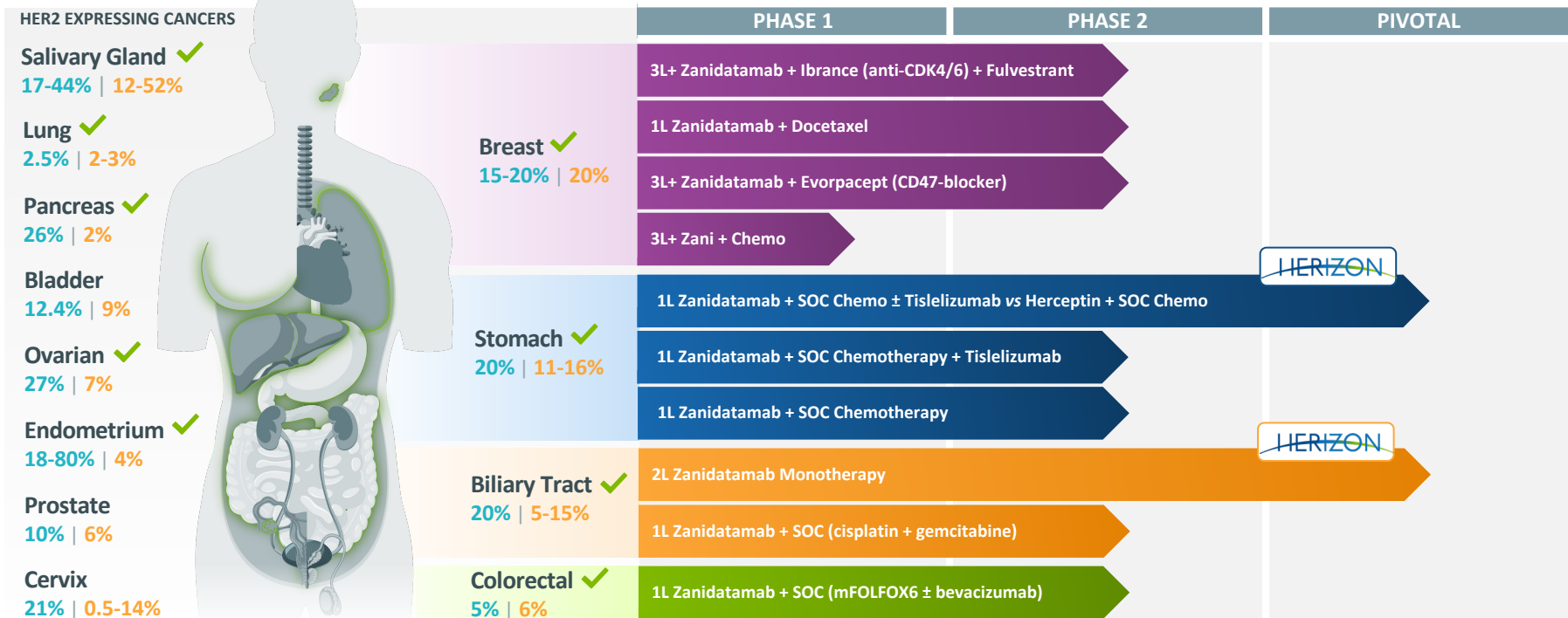


*The geometry of zanidatamab prevents it from binding to the same HER2 molecule*

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

# Broad Opportunity for Zanidatamab in HER2-Targeted Therapy

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

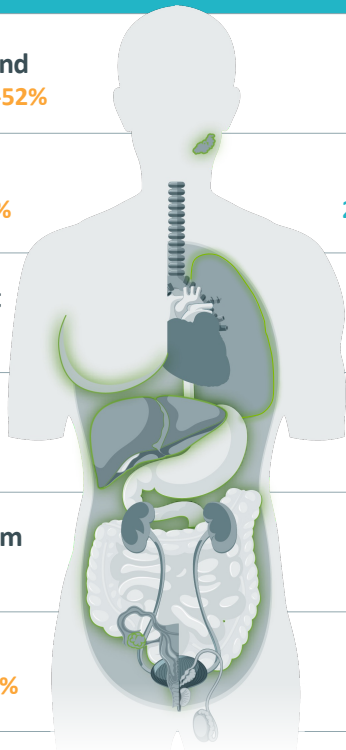


HER2 EXPRESSION | AMPLIFICATION  
 ✓ ZANIDATAMAB SINGLE AGENT ACTIVITY

SOC = Standard of Care

# Patient Populations Support Broad Opportunity Set

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



<sup>1</sup>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.

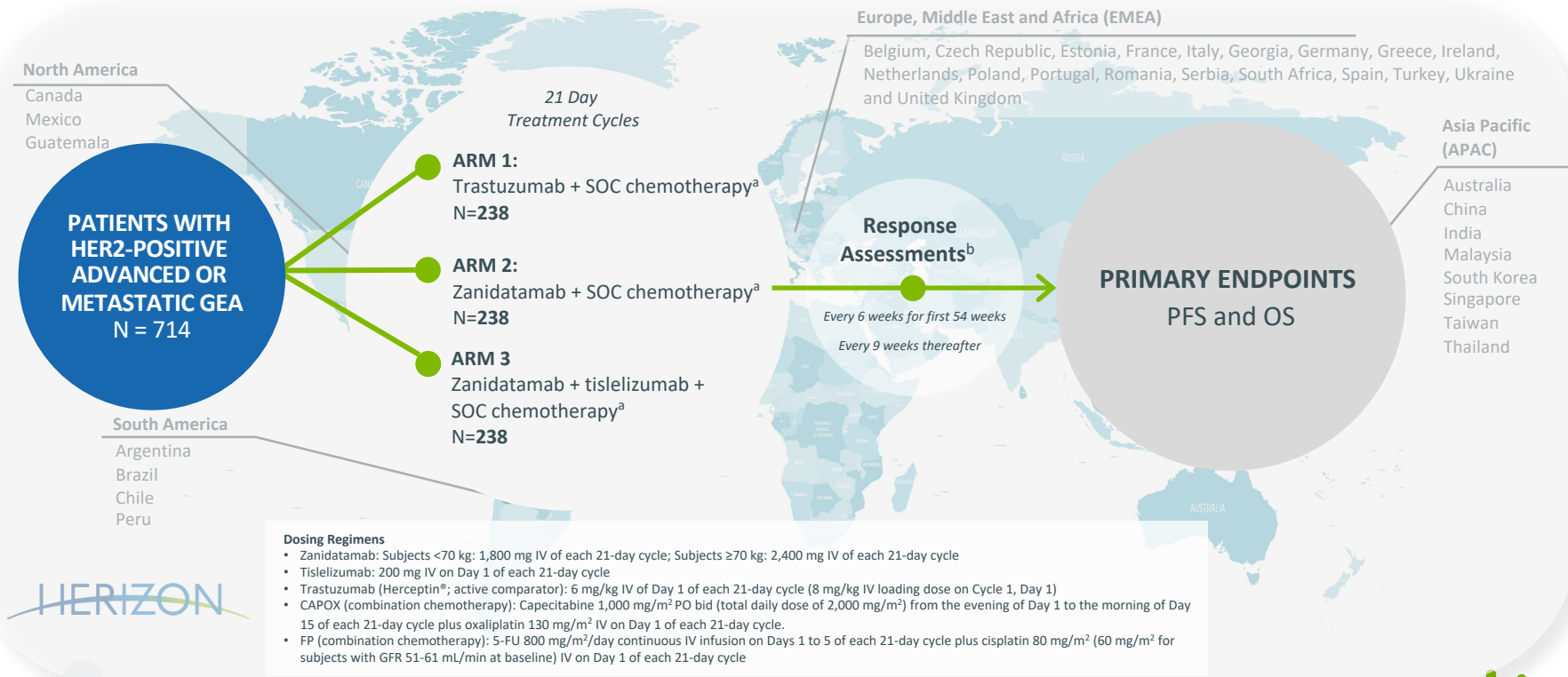
<sup>2</sup>ToGA Trial; Yan M, et al., Cancer Metastasis Rev (2015); Meric-Bernstam et al., Clinical Cancer Research (2018); <sup>3</sup>Roche Diagnostics biomarker data; S Pillai RN et al Cancer 2017; 123:4099-4105, Arcila ME et al Clin Cancer Res. 2012; 18: 4910-4918, Mazieres J et al J Clin Oncol. 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.



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

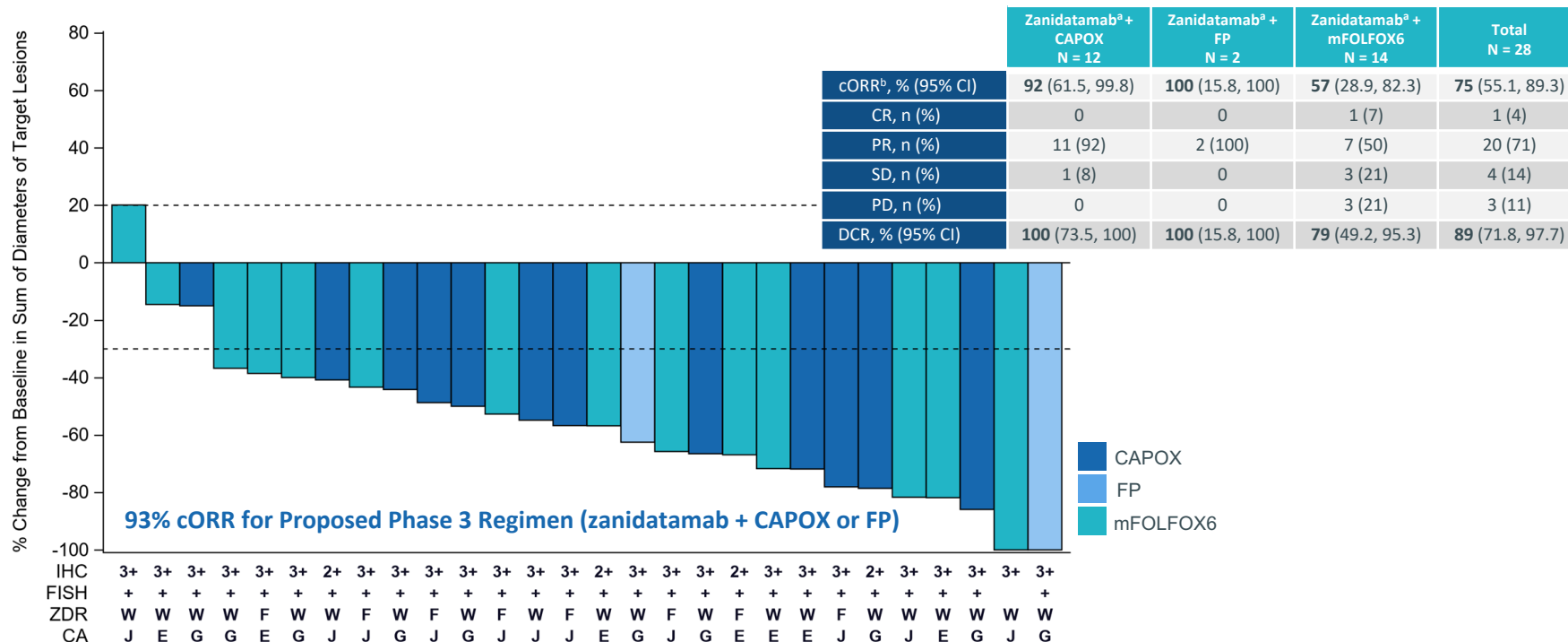
Study plans to enroll 714 patients at approximately 300 sites across 38 countries and is expected to complete enrollment in 2023



# Zanidatamab Plus Chemotherapy in HER2+ First-Line GEA

As reported at ESMO | Sep 2021

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



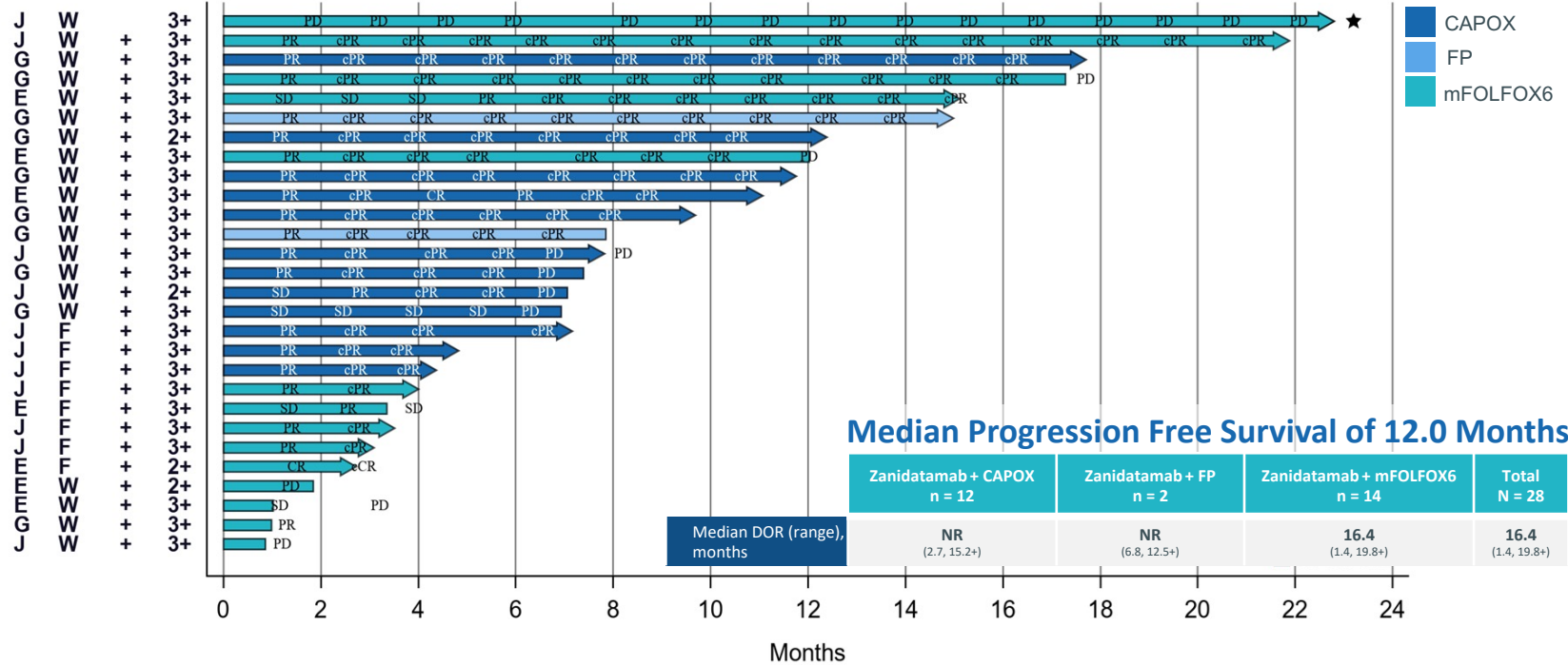
<sup>a</sup>HER2-positive was defined as IHC 3+ or IHC 2+/FISH+. <sup>b</sup>cORR included a baseline scan and a confirmatory scan obtained ≥ 4 weeks following initial documentation of objective response; the efficacy-evaluable population was defined as all HER2-positive subjects who had ≥ 1 evaluable 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.

# Zanidatamab Plus Chemotherapy in HER2+ First-Line GEA

As reported at ESMO | Sep 2021

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

CA ZDR FISH IHC



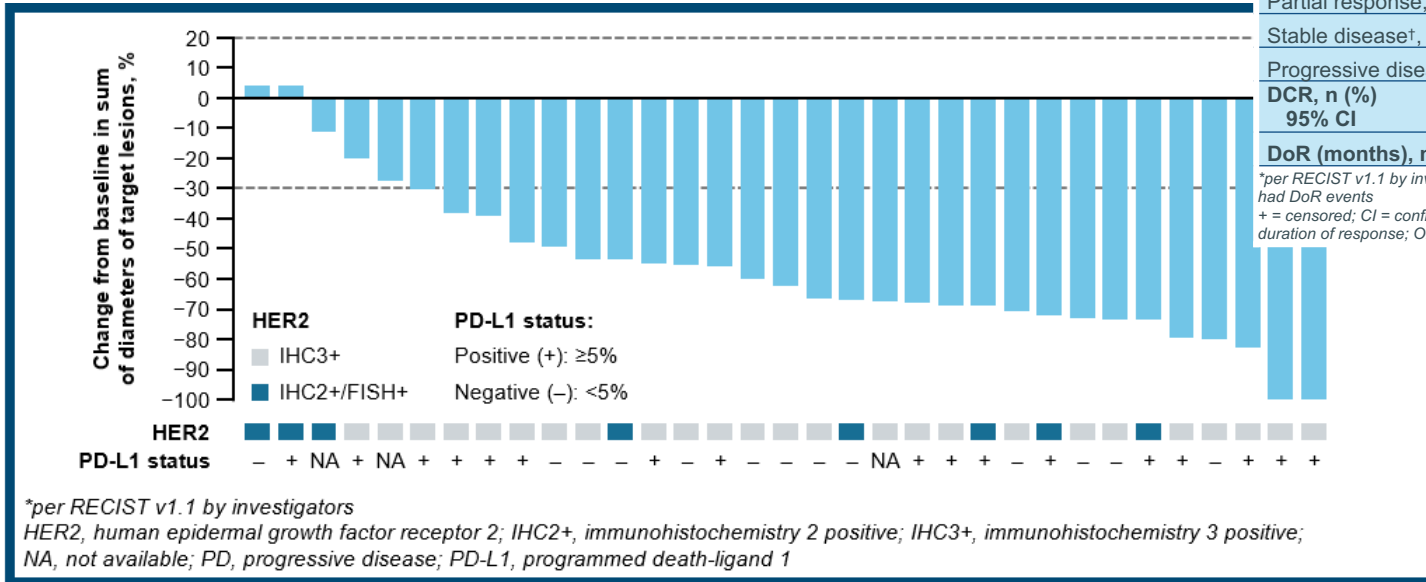
★ An MRI performed for neurologic symptoms on Day 8 demonstrated brain metastases, which were treated with radiation therapy. Subject remained on mFOLFOX6-1 with zanidatamab and has had long term disease control since treatment of brain metastases.

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.

# 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

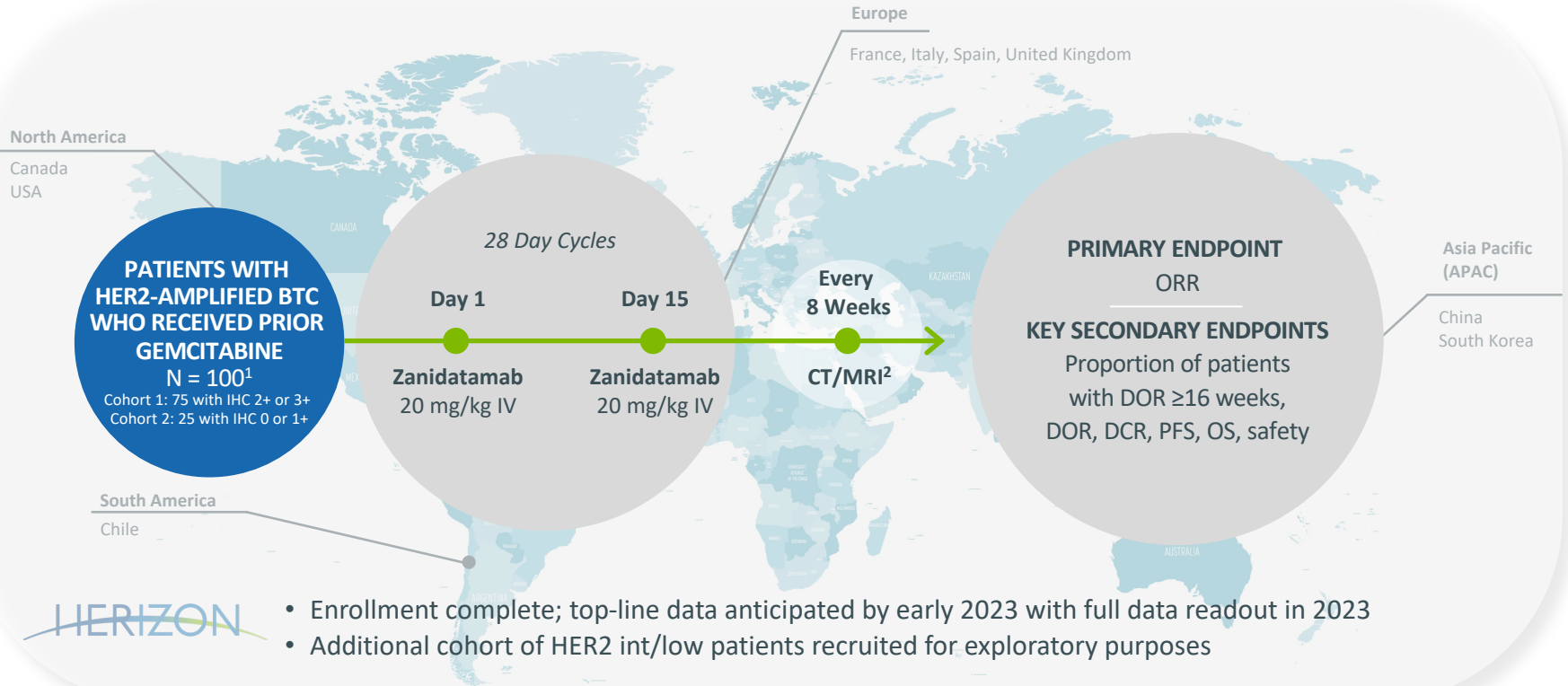


**Table 3. Disease response\***

	Total (N=33)
<b>Confirmed ORR, n (%)</b>	<b>25 (75.8)</b>
<b>95% CI</b>	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)
<b>DCR, n (%)</b>	<b>33 (100.0)</b>
<b>95% CI</b>	89.4, 100.0
<b>DoR (months), min, max†</b>	<b>2.1+, 18.2+</b>

\*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

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

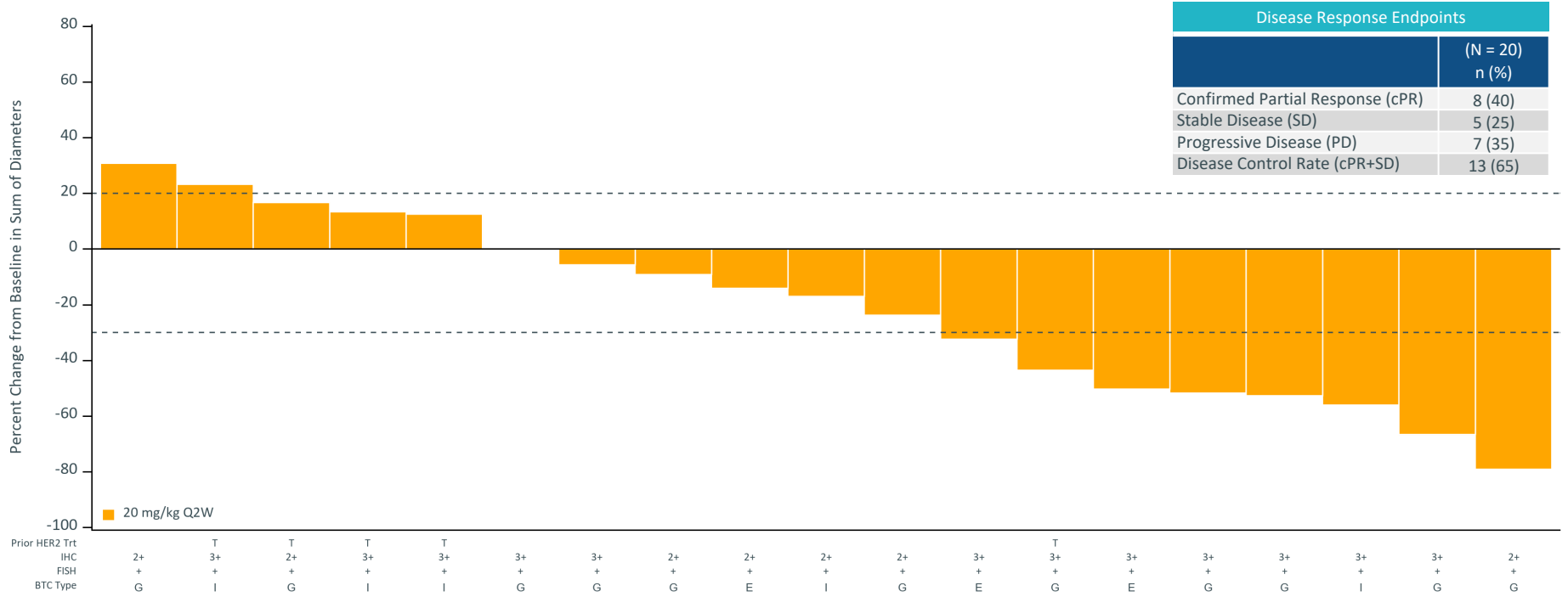


BTC: biliary tract cancer; DCR: disease control rate; DOR: duration of response; IHC: immunohistochemistry; IV: intravenous; MRI: magnetic resonance imaging; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; Q2W: every 2 weeks; RECIST: Response Evaluation Criteria in Solid Tumors.  
<sup>1</sup>All patients on study are HER2-amplified as determined by in-situ hybridization (ISH) assay.  
<sup>2</sup>For tumor assessment per RECIST v1.1.2.

# 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



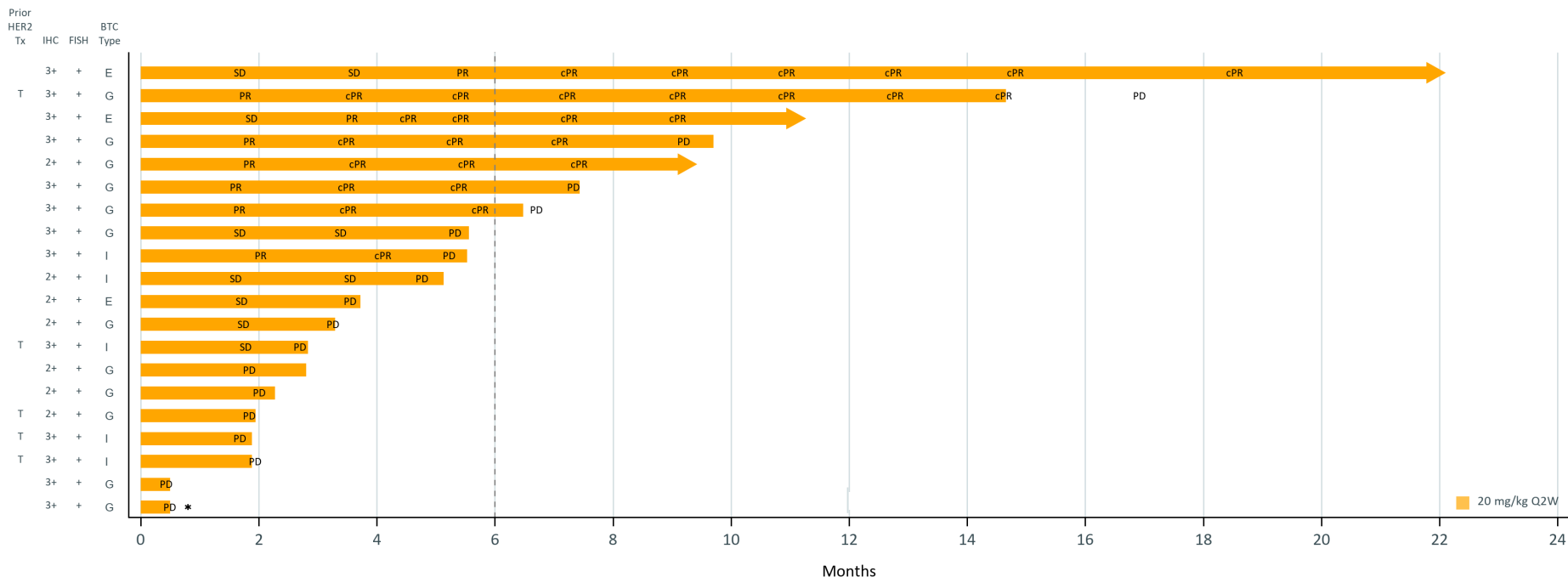
E: Extrahepatic Cholangiocarcinoma; FISH: fluorescence in situ hybridization; I: Intrahepatic Cholangiocarcinoma; IHC: immunohistochemistry; G: Gallbladder; T: trastuzumab; Trt: treatment. Response-evaluable: all treated patients with measurable disease who had at least one evaluable, post-baseline disease 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.



# 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)

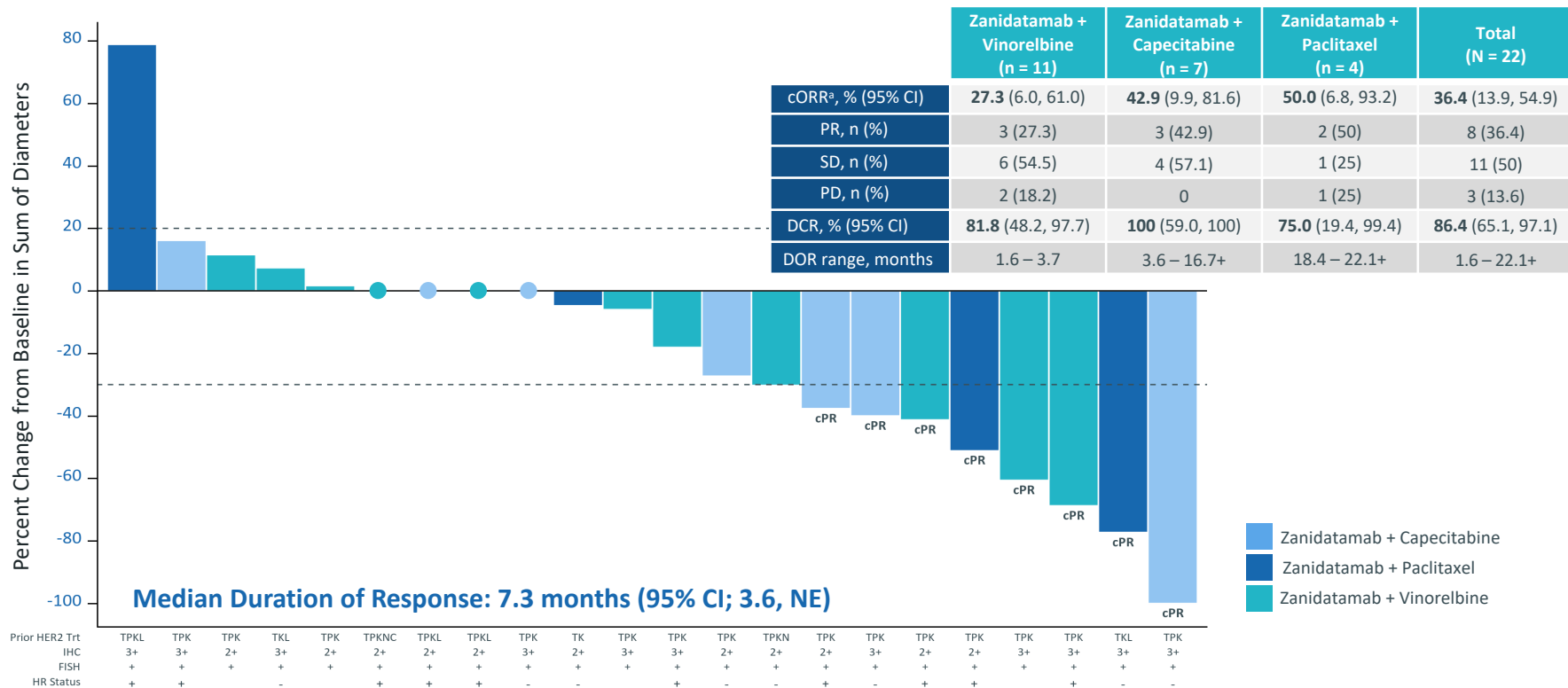


(c)PR: (confirmed) partial response; E: extrahepatic cholangiocarcinoma, FISH: fluorescence in situ hybridization; I: intrahepatic cholangiocarcinoma, IHC: immunohistochemistry; G: gallbladder; PR: partial response; PD: progressive disease; SD: stable disease; T: trastuzumab; Tx: Treatment. \*, death.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

# Zanidatamab Plus Chemotherapy in HER2+ Third-Line+ Breast Cancer

As reported at SABCS | Dec 2021

## Promising Antitumor Activity Observed in Heavily Pretreated Breast Cancer Patients



C: tucatinib; cORR: confirmed objective response rate; cPR: confirmed partial response; DOR: duration of response; DCR: disease control rate; FISH: fluorescence in situ hybridization; HR: hormone receptor; IHC: immunohistochemistry; K: T-DM1; L: lapatinib; N: neratinib; P: pertuzumab; T: trastuzumab; Trt: treatment



# 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

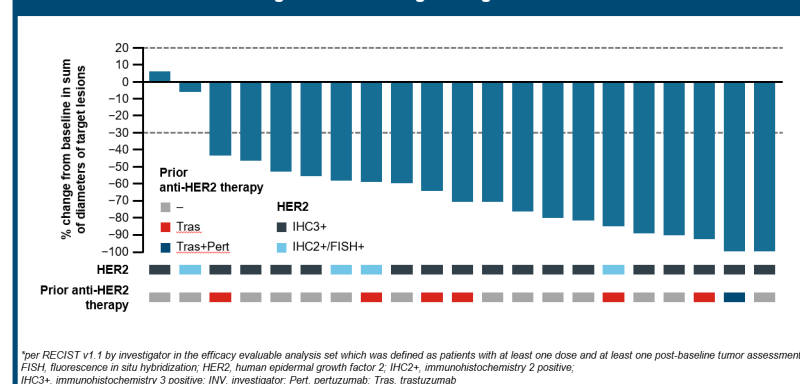
- Of the 21 efficacy evaluable patients, the confirmed objective response rate (ORR) was 90.5% (95% CI: 69.6, 98.8) (Table 3) with 15 patients (78.9%) who were ongoing responders.
- The disease control rate was 95.2% (95% CI: 76.2, 99.9) (Table 3); 20 patients had controlled disease
- The 6-month progression-free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

Table 3. Disease response\*

	Total (N=21)
cORR <sup>†</sup> , %	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 <sup>†</sup> , %	95.2
95% CI	76.2, 99.9
DoR (months), min, max <sup>‡</sup>	1.4+, 12.4

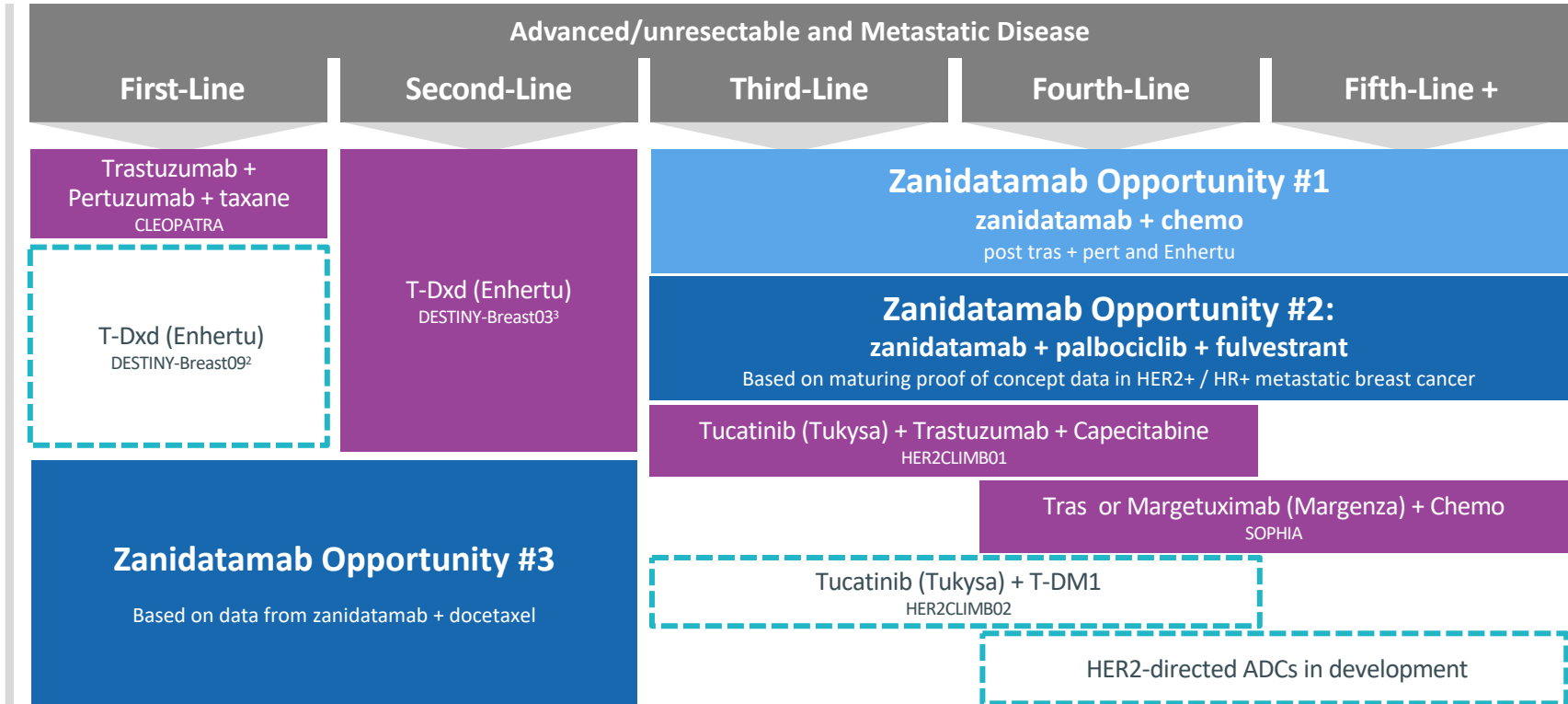
\*In the efficacy evaluable analysis set; <sup>†</sup>per RECIST v1.1 by investigators; <sup>‡</sup>15.8% of patients had DoR events +, censored; CI, confidence interval; cORR, confirmed objective response rate; DCR, disease control rate; DoR, duration of response

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

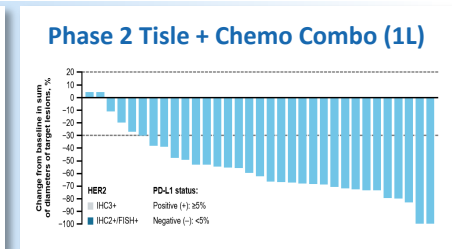
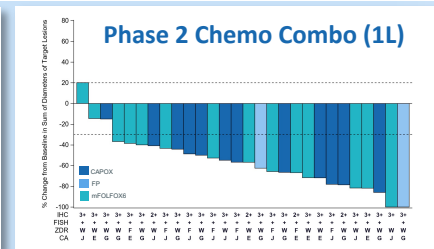
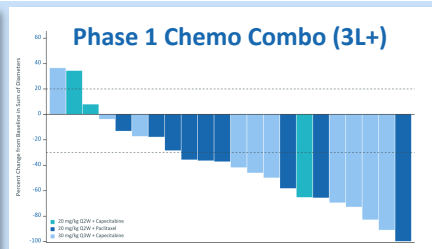
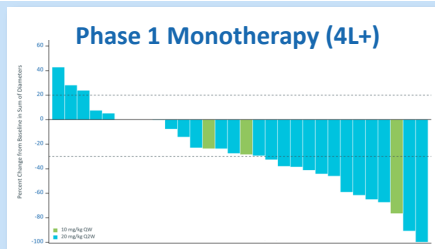
# Significant Opportunity for Zanidatamab in HER2+ mBC



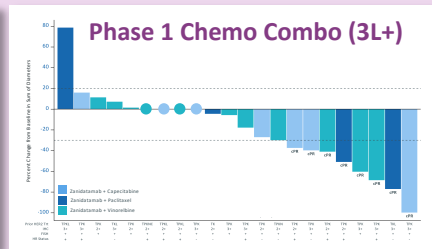
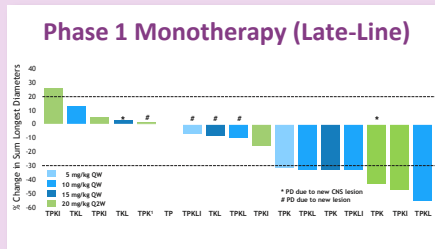
Investigational

# Breadth of Zanidatamab Clinical Data

## Gastroesophageal

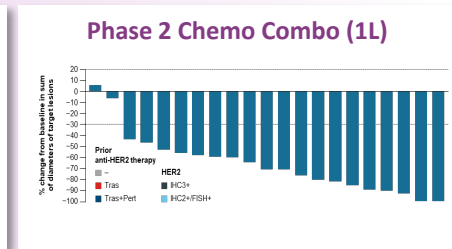


## Breast Cancer

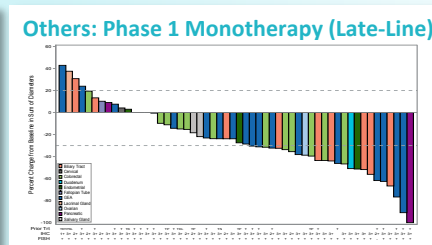
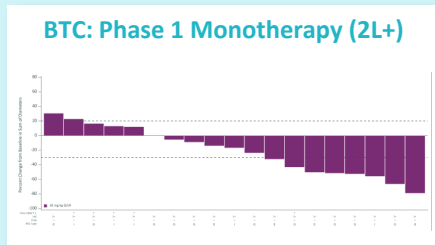


### Phase 2 CDK4/6 Combo (3L+)

4Q 2022<sup>1</sup>



## Other Solid Tumors



Gastroesophageal: [Phase 1 Monotherapy \(4L+\)](#), [Phase 1 Chemo Combo \(3L+\)](#), [Phase 2 Chemo Combo \(1L\)](#), [Phase 2 Tisle + Chemo Combo \(1L\)](#)

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 \(Late-Line\)](#)

<sup>1</sup> Data anticipated to be presented in the fourth quarter 2022

# BeiGene Clinical & Commercial Collaboration Overview



## Partnership Highlights

- BeiGene has development and commercial rights to zanidatamab and ZW49 in Asia-Pacific region (excluding Japan and India)
- Zymeworks retains full rights outside of BeiGene's territory and continues to lead global development for both programs
- Collaborate on certain global studies including HERIZON-BTC-01 and HERIZON-GEA-01 with BeiGene responsible for clinical and regulatory activities in their territory

## Financials

- Upfront: \$40 million
- Milestones: up to \$390 million
- Milestones received to date: more than \$20 million
- Royalties: tiered up to 20% on sales in BeiGene territory

# Zanidatamab Zovodotin (ZW49): A Biparatopic ADC for HER2-Targeted Therapy

## Unique Mechanisms of Action

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

## Clinical Data Highlights





















- Differentiated safety profile with the majority of adverse events grade 1 or 2 and are reversible and manageable
- Multiple confirmed responses observed across several tumor types
- Completed enrollment for expansion cohort targeting 2.5 mg/kg 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 ZW49 Catalysts

- Complete expansion cohorts for both weekly and every three week dosing regimens & define Phase 2 clinical development plan
- Report Phase 1 clinical data and recommended Phase 2 dose at medical meeting in H2 2022



# Technology Validated by Platform Partnerships & Collaborations

PROGRAMS   PLATFORMS	PRECLINICAL	PHASE 1	PHASE 2	COMMERCIAL RIGHTS
<b>PARTNERSHIPS</b>				
Bispecific Antibody		Oncology		
XB002 (ICON-2) Tissue Factor ADC		Solid Tumors		
JNJ-78278343 CD3 x KLK2 Bispecific		Castration-Resistant Prostate Cancer		
JNJ-78306358 CD3 x HLA-G Bispecific		Solid Tumors		
ATRC-301 EphA2 Targeting ADC		Oncology		
Bispecific Antibody		Undisclosed		
Bispecific Antibody		Immuno-Oncology		
Bispecific Antibody		Infectious Disease/Undisclosed		
Bispecific Antibody		Dermatology		
Bispecific Antibody		Undisclosed		



\*Original Agreement with Celgene (which is now a Bristol-Myers Squibb company)

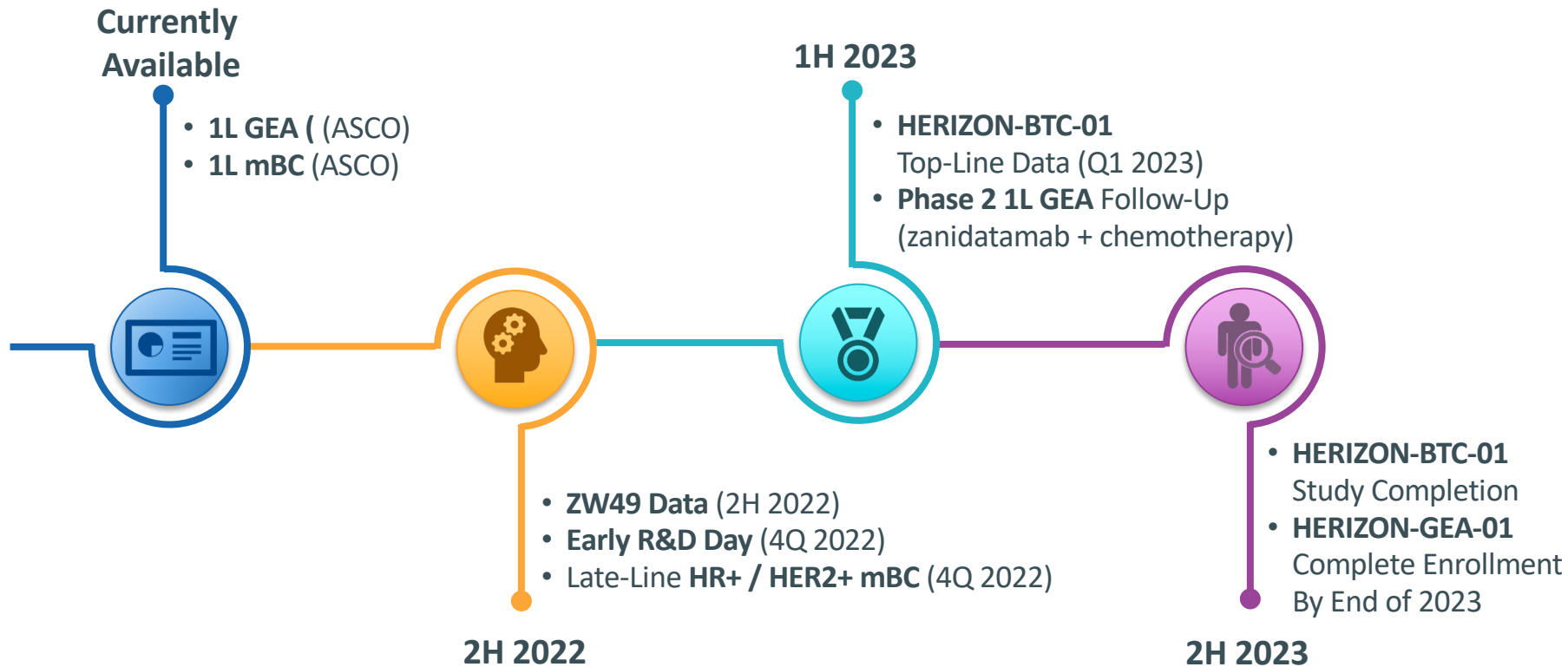
\*\*Original Agreement with Iconic; XB002 in-licensed by Exelisis

# Key Strategic Priorities for 2022 and 2023

KEY STRATEGIC PRIORITIES	STATUS / TARGET
<b>Financial</b>	
Reduction in workforce	✓
Improve financial position	✓
Monetize existing financial and preclinical assets	Ongoing
<b>Clinical</b>	
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	H2 2022
<b>Preclinical and Platforms</b>	
Update on progress of early-stage R&D programs	Q4 2022
Advance two new product candidate to IND stage	YE 2024
<b>Partnerships &amp; Collaborations</b>	
Execute new partnerships and collaborations	Ongoing

- Priority is to **reset** and **focus** the company on maximizing shareholder value and patient outcomes
- **Advance enrollment** of existing zanidatamab pivotal trials and identify future development paths for zanidatamab and ZW49
- **Aggressively pursue** and **drive value** through partnerships and collaborations
- **Continually improve financial position** through non-dilutive funding sources

# Anticipated Upcoming Data Catalysts





# Key Investment Highlights

**Near-term market opportunity** with zanidatamab in GEA and BTC with additional clinical indications to support market expansion

**R&D Pipeline** driven by next-generation ADC and multi-specific platforms

**Additional upside** with ZW49 clinical program and near-term **partnership opportunities**

- Strategic priorities underpinned by **new management team, improved financial position** with **cash runway into 2H23**, and **portfolio of existing partnership and collaborations**
- Management **focused on further extending cash runway** into 2024 via **non-dilutive monetization and partnerships** to further facilitate strategic priorities
- **Execution on new and existing partnerships** as strategy for **non-dilutive funding** and **expansion** of zanidatamab into additional indications that suit tolerability and combinability profile

# Company Contacts

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