



H.C. Wainwright 24th Annual Global Investment Conference

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NYSE: ZYME

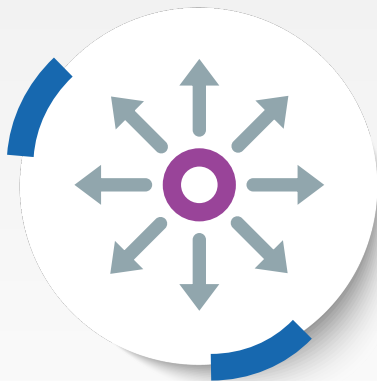
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This presentation includes “forward-looking statements” within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and “forward-looking information” within the meaning of Canadian securities laws, or collectively, forward looking statements. Forward-looking statements 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
- TOP01i 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

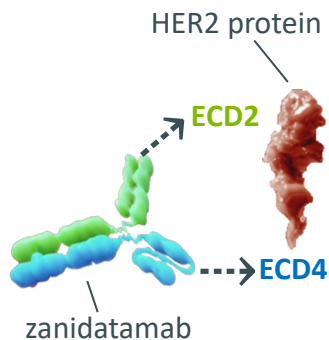
Integrated Platforms Drive Growing Candidate Pipeline

PROGRAMS COMMERCIAL RIGHTS		TARGET	PRECLINICAL	PHASE 1	PHASE 2	PIVOTAL
LEAD PRODUCT CANDIDATES						
Zanidatamab <i>HER2 X HER2 Bispecific</i>		HER2	Biliary Tract Cancer <i>FDA Breakthrough Therapy designation</i> HERIZON-BTC-01			
 		HER2	Gastroesophageal Adenocarcinomas HERIZON-GEA-01			
		HER2	Breast Cancer			
		HER2	HER2-Expressing Solid Tumors			
Zanidatamab Zovodotin (ZW49) <i>HER2 X HER2 Bispecific ADC</i>		HER2	HER2-Expressing Solid Tumors			
 						
PRECLINICAL PROGRAMS						
ZW191 <i>TOPO1i ADC</i>		Undisclosed	OVCA, Gynecological			
ZW171 <i>2+1 T-Cell Engaging Bispecific</i>		Undisclosed	Solid Tumors			

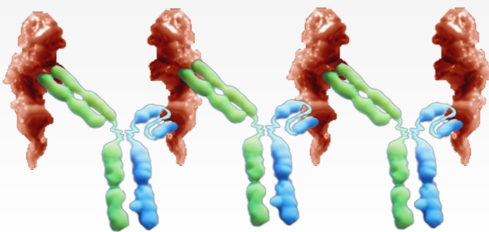
Zanidatamab: A Biparatopic Bispecific Antibody for HER2-Expressing Cancers

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

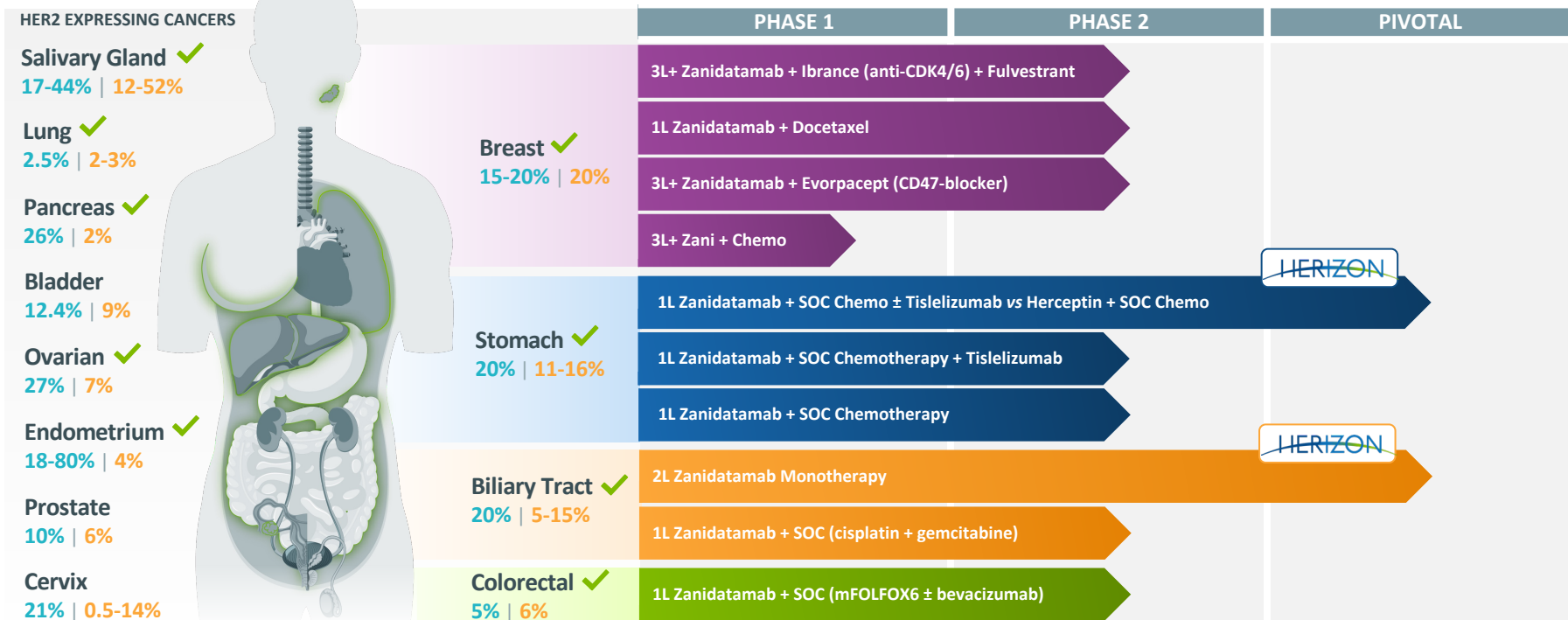


The geometry of zanidatamab prevents it from binding to the same HER2 molecule

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

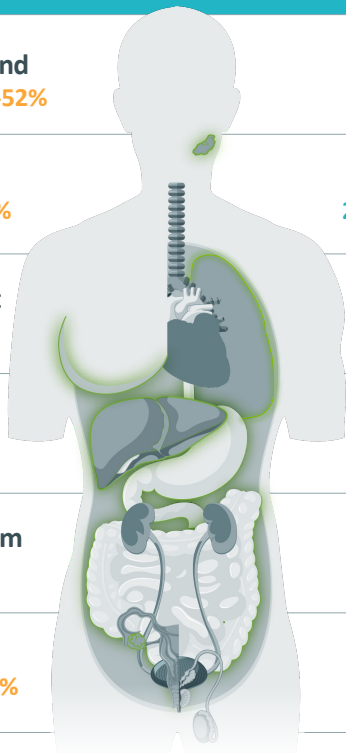


HER2 EXPRESSION | AMPLIFICATION
 ✓ ZANIDATAMAB SINGLE AGENT ACTIVITY

SOC = Standard of Care

Patient Populations Support Broad Opportunity Set

Estimated HER2+ Patient Population ¹	ZANIDATAMAB SINGLE AGENT ACTIVITY	HER2 EXPRESSION AMPLIFICATION		ZANIDATAMAB SINGLE AGENT ACTIVITY	Estimated HER2+ Patient Population ¹
HER2 EXPRESSING CANCERS					
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



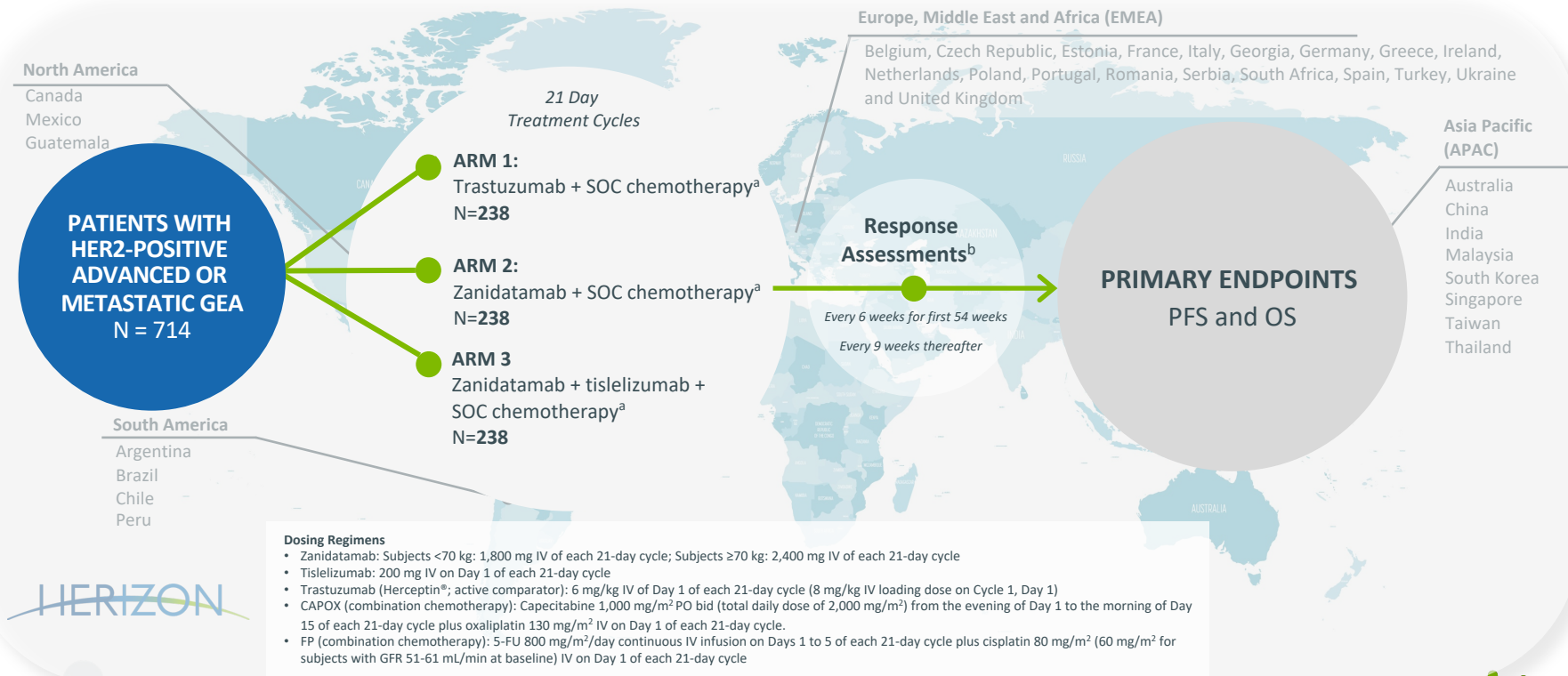
¹Estimates rounded to nearest hundred patients and averaged where represented by a range of expression / amplification; represent potential HER2+ patients by indication for US, EU28, and Japan; excludes BeiGene controlled commercial territories.

²ToGA Trial; Yan M, et al., Cancer Metastasis Rev (2015); Meric-Bernstam et al., Clinical Cancer Research (2018); ³Roche Diagnostics biomarker data; 5 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

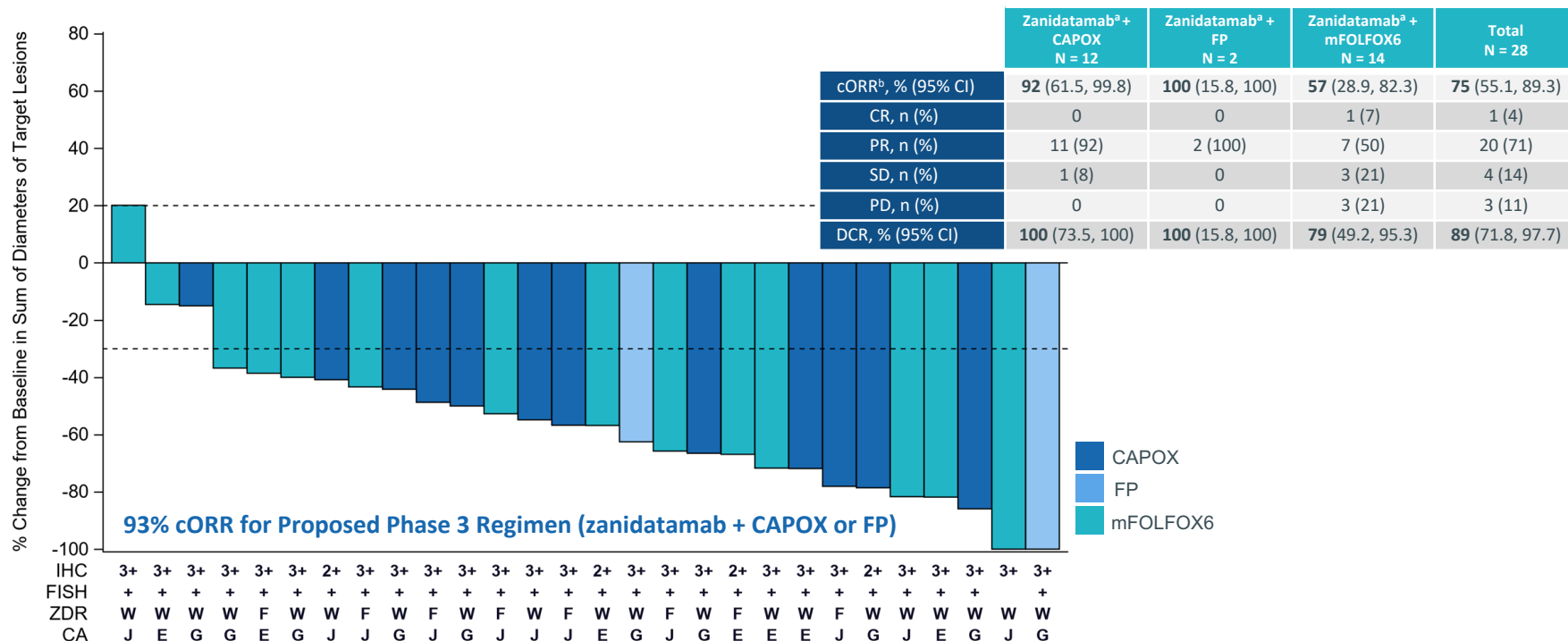
Study plans to enroll 714 patients at approximately 300 sites across 38 countries and is expected to complete enrollment in 2023



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



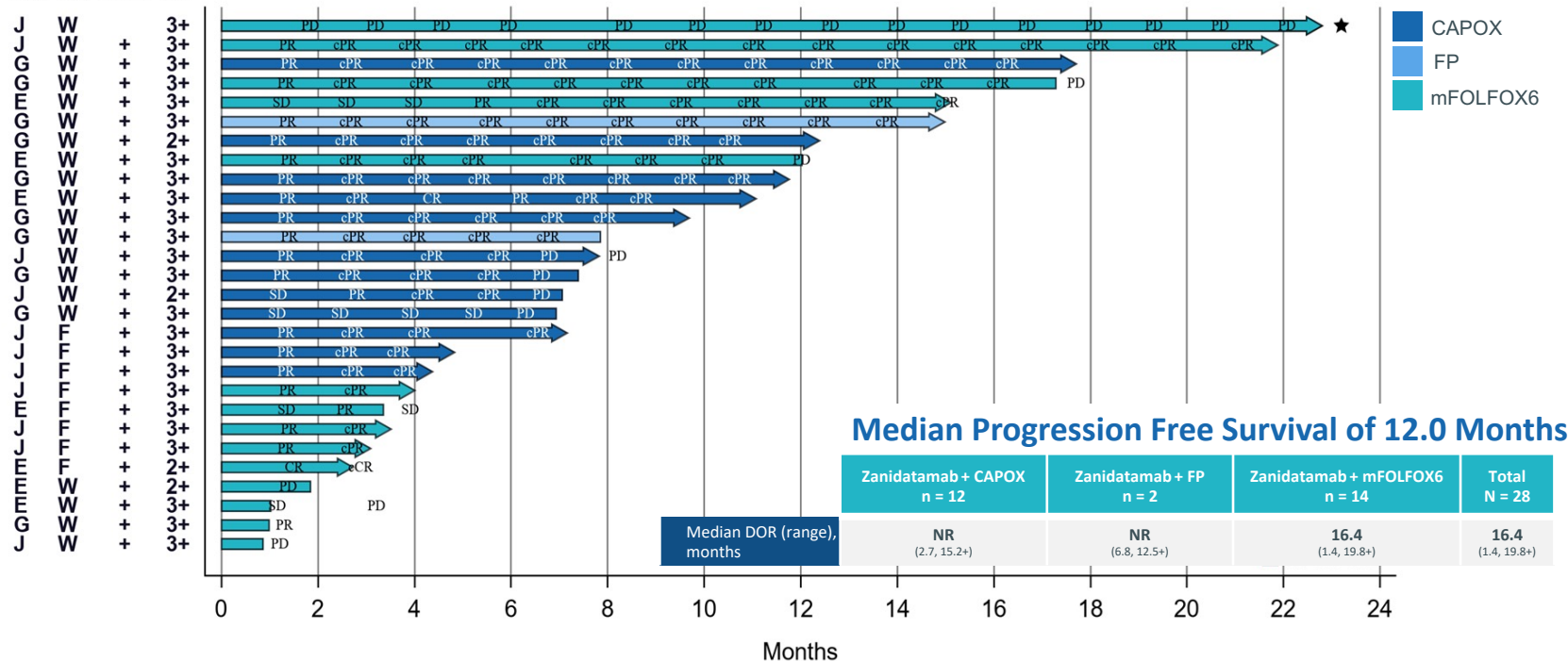
^aHER2-positive was defined as IHC 3+ or IHC 2+/FISH+. ^bcORR included a baseline scan and a confirmatory scan obtained ≥ 4 weeks following initial documentation of objective response; the efficacy-evaluable population was defined as all HER2-positive subjects who had ≥ 1 evaluable post-baseline disease 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

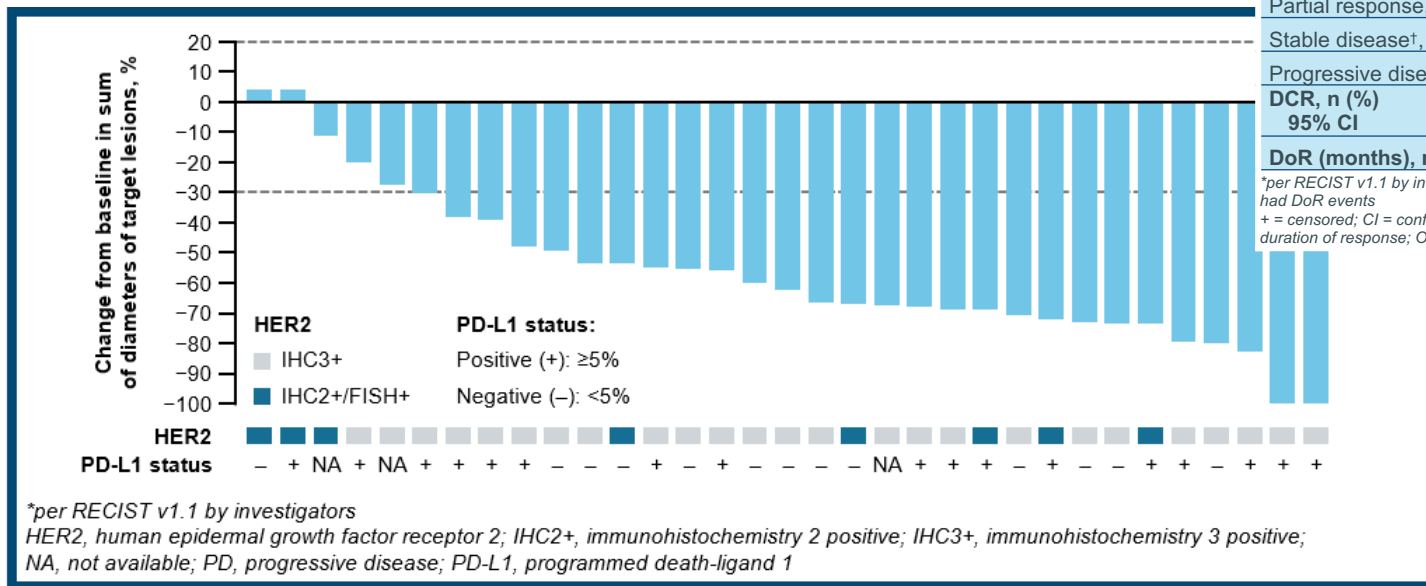


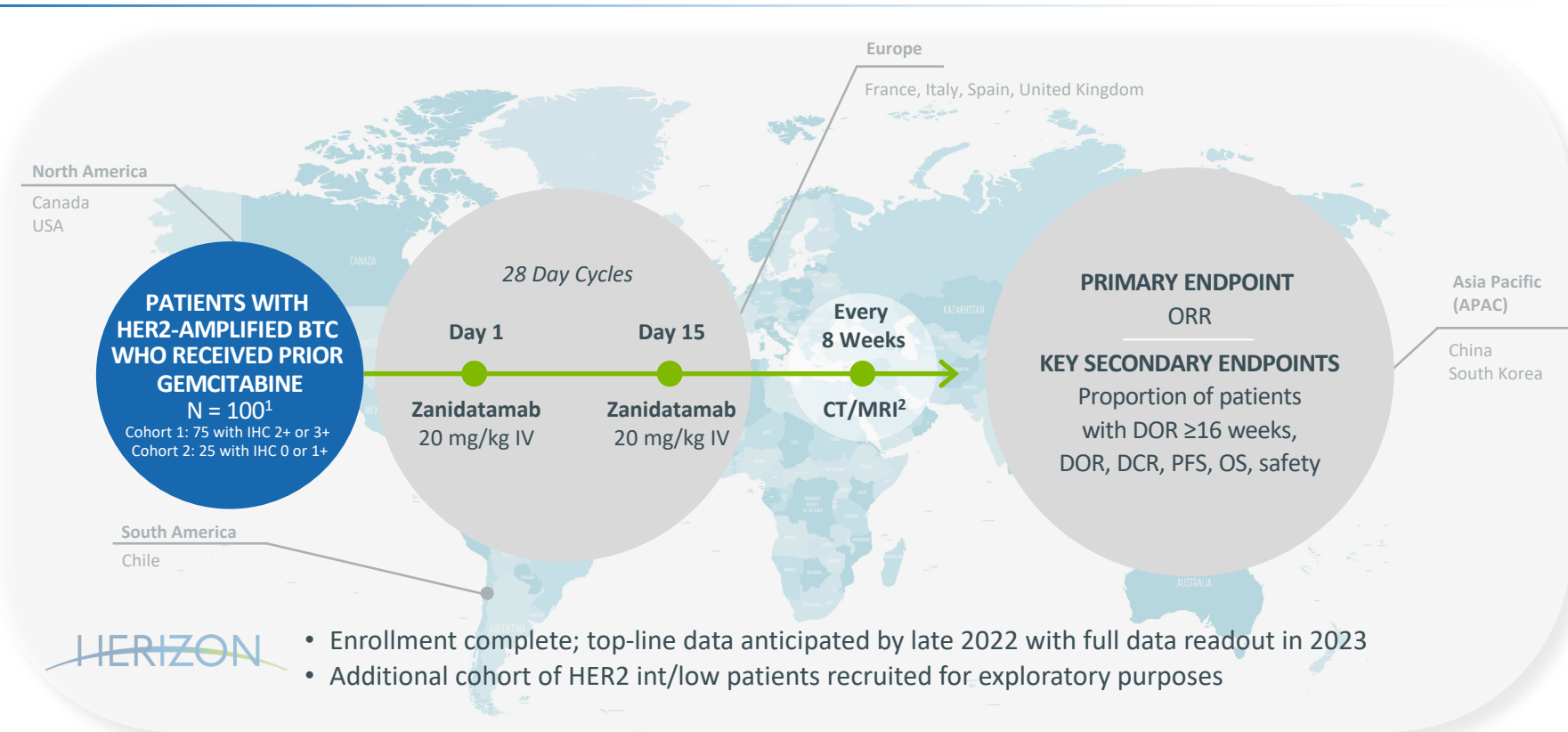
Table 3. Disease response*

	Total (N=33)
Confirmed ORR, n (%)	25 (75.8)
95% CI	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 (%)	33 (100.0)
95% CI	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

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.

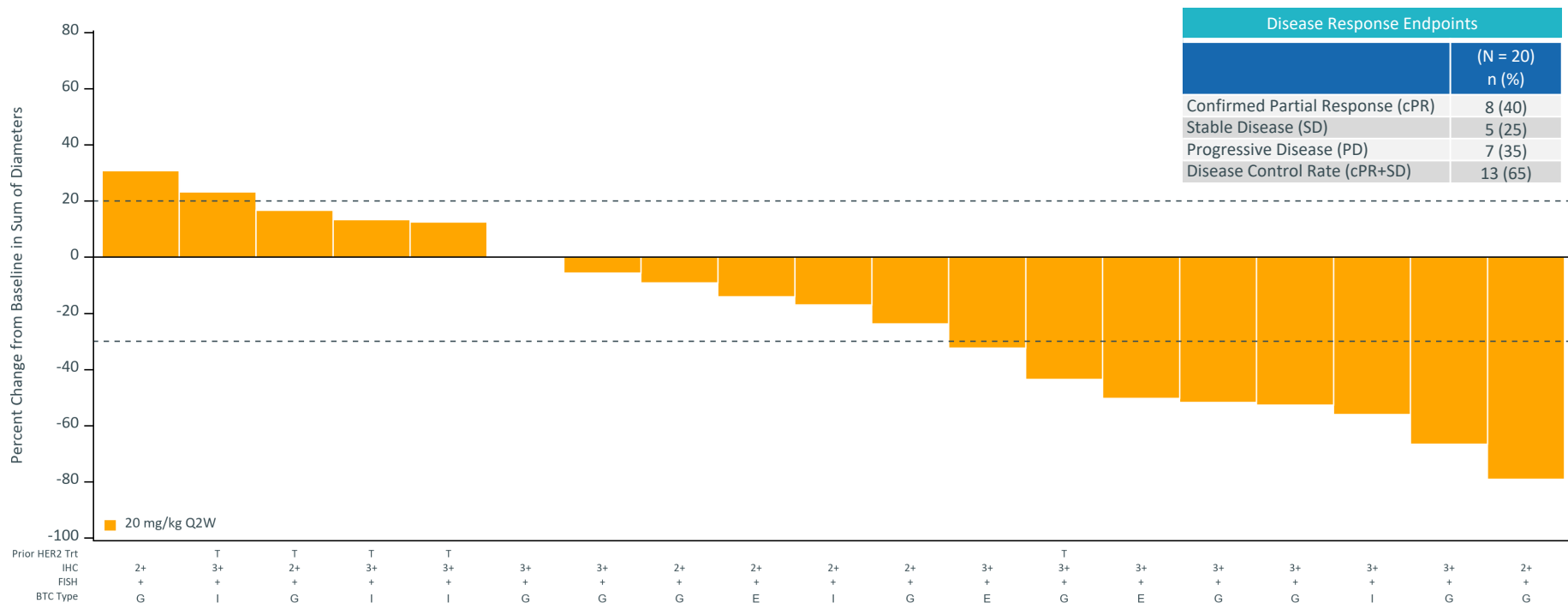
¹All patients on study are HER2-amplified as determined by in-situ hybridization (ISH) assay.

²For 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



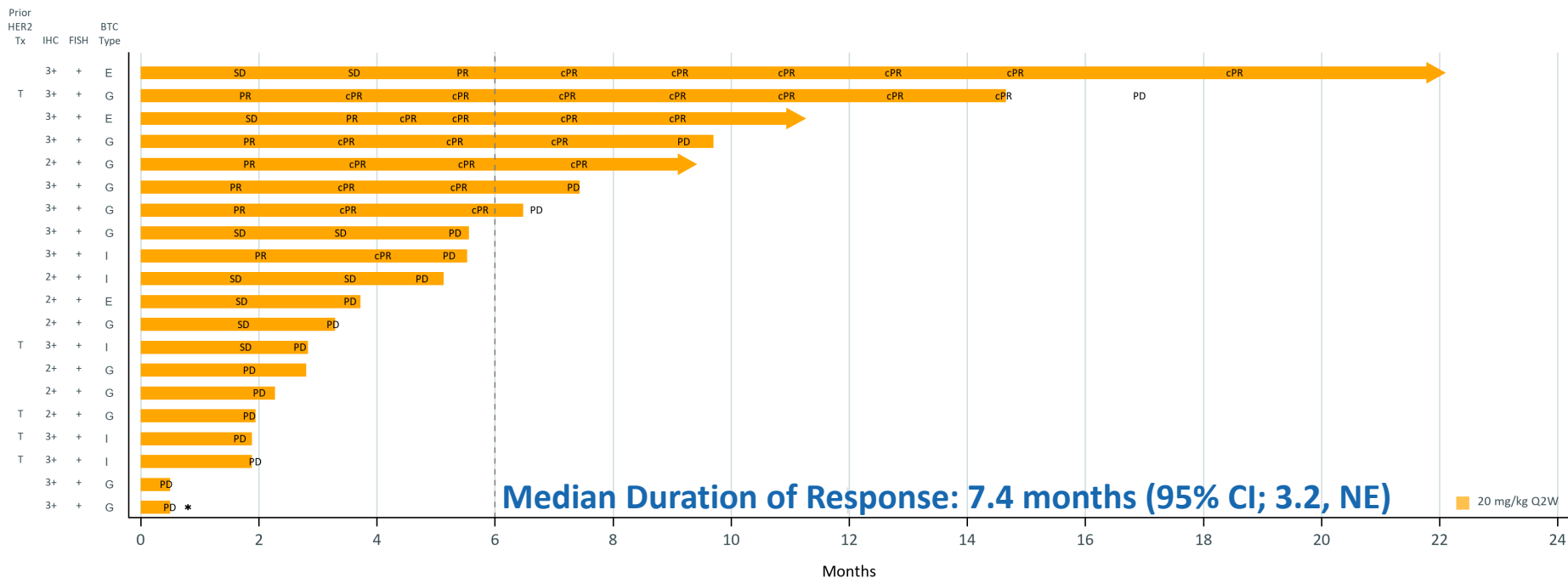
E: Extrahepatic Cholangiocarcinoma; FISH: fluorescence in situ hybridization; I: Intrahepatic Cholangiocarcinoma; IHC: immunohistochemistry; G: Gallbladder; T: trastuzumab; Trt: treatment.
Response-evaluable: all treated patients with measurable disease who had at least one evaluable, post-baseline disease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

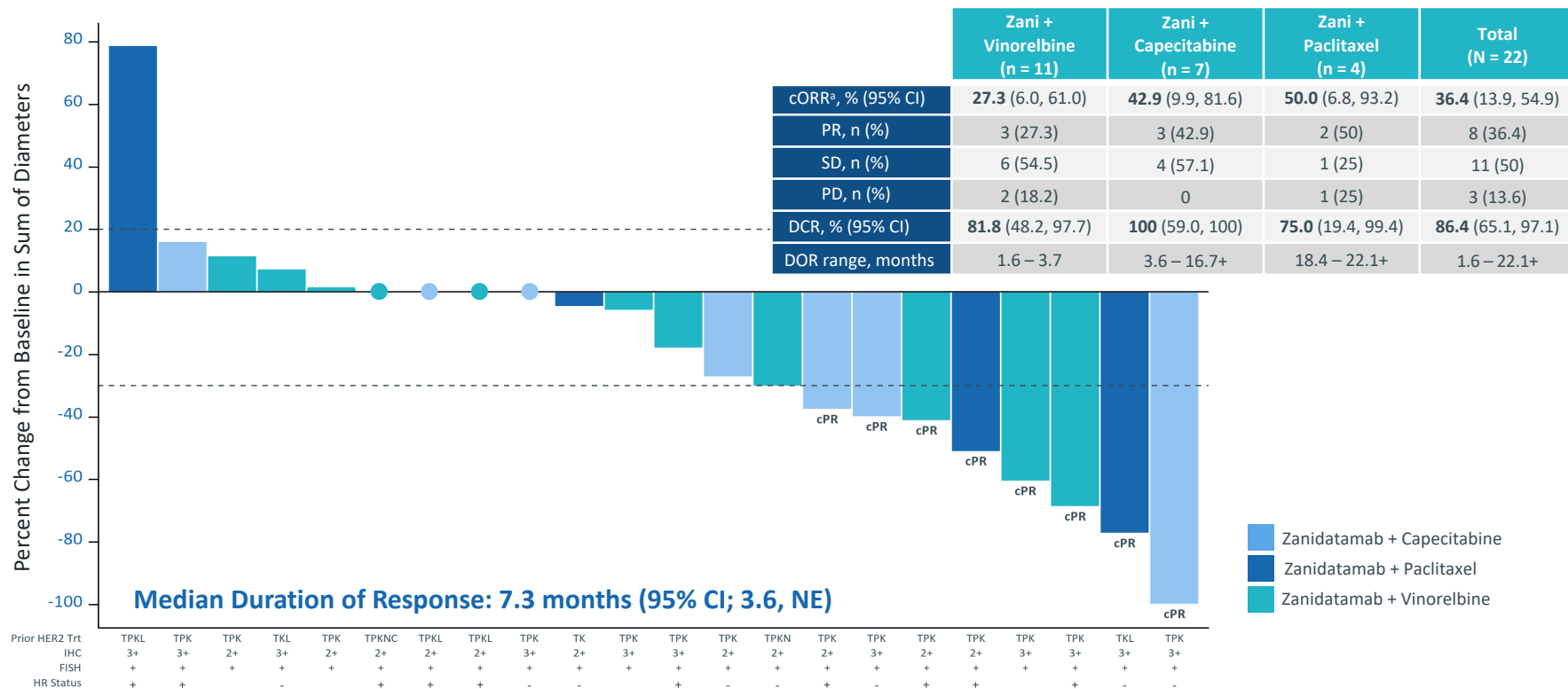


(c)PR: (confirmed) partial response; E: extrahepatic cholangiocarcinoma, FISH: fluorescence in situ hybridization; I: intrahepatic cholangiocarcinoma, IHC: immunohistochemistry; G: gallbladder; PR: partial response; PD: progressive disease; SD: stable disease; T: trastuzumab; Tx: Treatment. *, death.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

Zanidatamab Plus Chemotherapy in HER2+ 3L+ Breast Cancer

As reported at SABCS | Dec 2021

Promising Antitumor Activity Observed in Heavily Pretreated Breast Cancer Patients



C: trastuzumab; 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

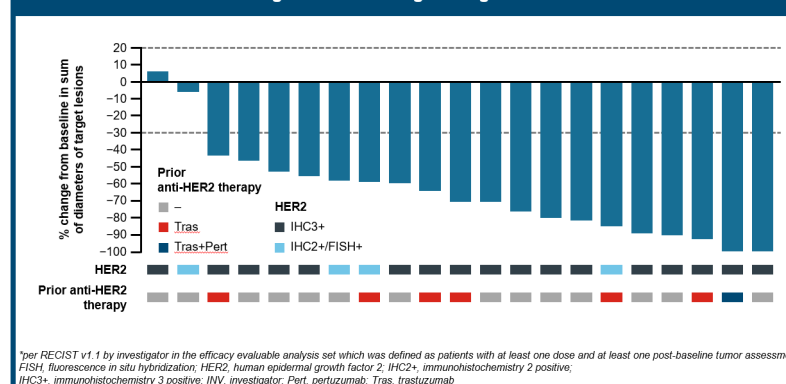
- Of the 21 efficacy evaluable patients, the confirmed objective response rate (ORR) was 90.5% (95% CI: 69.6, 98.8) (Table 3) with 15 patients (78.9%) who were ongoing responders.
- The disease control rate was 95.2% (95% CI: 76.2, 99.9) (Table 3); 20 patients had controlled disease
- The 6-month progression-free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

Table 3. Disease response*

	Total (N=21)
cORR†, %	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*

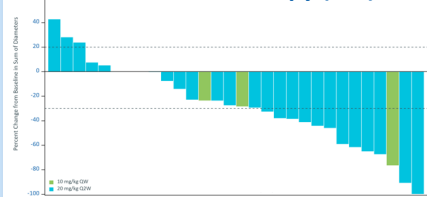


*per RECIST v1.1 by investigator in the efficacy evaluable analysis set which was defined as patients with at least one dose and at least one post-baseline tumor assessment
FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor 2; IHC2+, immunohistochemistry 2 positive; IHC3+,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

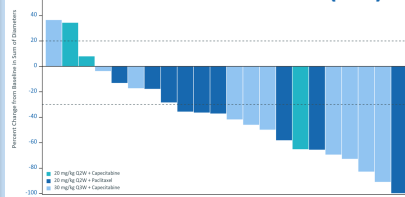
Breadth of Zanidatamab Clinical Data

Gastroesophageal

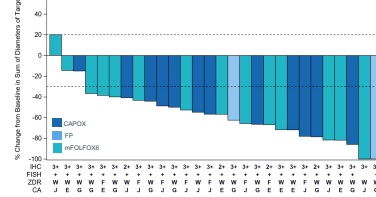
Phase 1 Monotherapy (4L+)



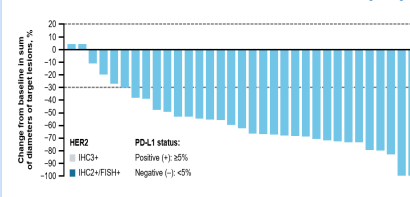
Phase 1 Chemo Combo (3L+)



Phase 2 Chemo Combo (1L)

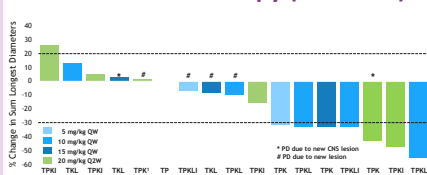


Phase 2 Tisle + Chemo Combo (1L)

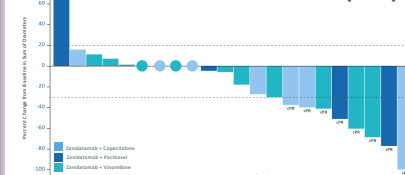


Breast Cancer

Phase 1 Monotherapy (Late-Line)



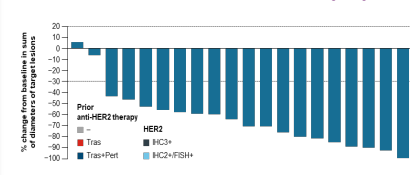
Phase 1 Chemo Combo (3L+)



Phase 2 CDK4/6 Combo (3L+)

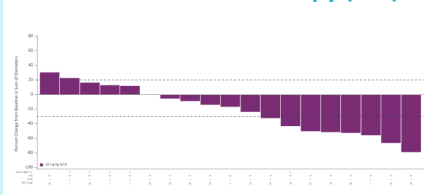
4Q 2022¹

Phase 2 Chemo Combo (1L)

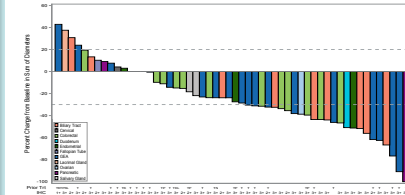


Other Solid Tumors

BTC: Phase 1 Monotherapy (2L+)



Others: Phase 1 Monotherapy (Late-Line)



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 \(Late-Line\)](#)

¹ 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 amongst HER2-targeted ADCs with the majority of adverse events being grade 1 or 2 and both reversible and manageable
- Confirmed ORR of 28%, disease control rate of 72% observed across 29 response-evaluable patients treated with ZW49 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 ZW49 Catalysts

- Investor webcast and conference call to discuss ESMO results at 4:30pm ET on September 12th
- Update on progression of weekly expansion and escalation cohorts
- Recommended Phase 2 dose to be announced 2H22



Technology Validated by Platform Partnerships & Collaborations

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			
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)

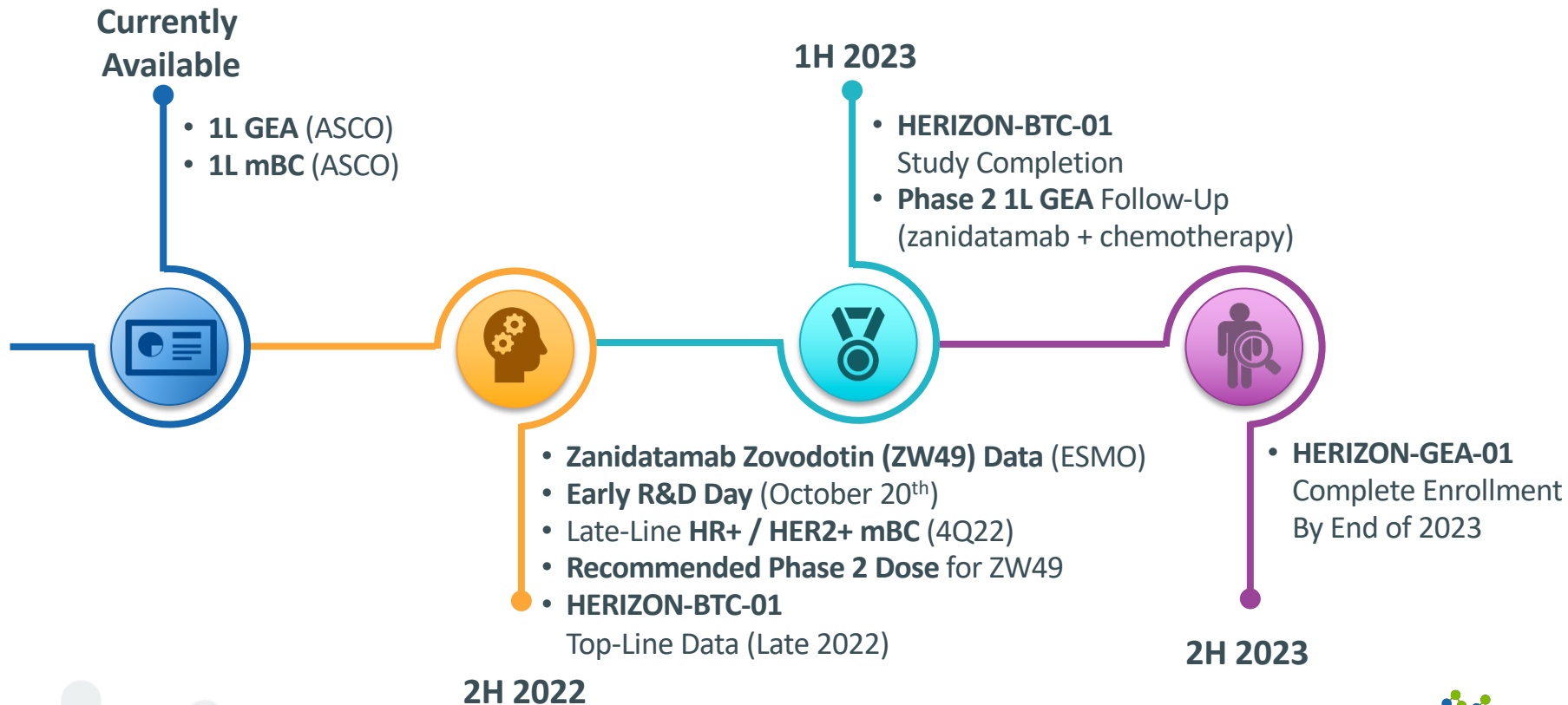
**Original Agreement with Iconic; XB002 in-licensed by Exelixis

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	ESMO
Preclinical and Platforms	
Update on progress of early-stage R&D programs	Oct 20 th , 2022
Advance two new product candidate to IND stage	YE 2024
Partnerships & Collaborations	
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

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



David Poon, Ph.D.
VP, Business Development
and Alliance Management



Daniel Dex, JD
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