



Barclays Global Healthcare Conference

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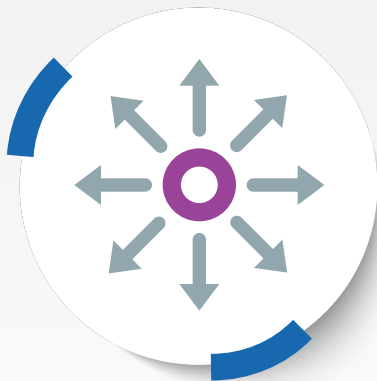
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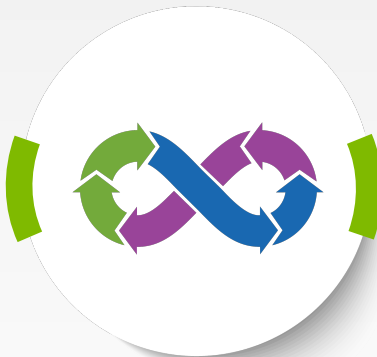


First-in-class and Best-in-class Multifunctional Therapeutics for Oncology



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 First & Best-in-Class 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

ZymeLink™

Next-Gen Drug Conjugate Platform



- Suite of proprietary auristatin and next-gen topo1i platform
- Stable, cleavable linkers
- IgG1-like PK and exposure
- Demonstrated tolerability
- Wide therapeutic window

EFECT™

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



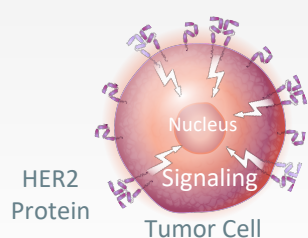
Zanidatamab: A Bispecific Antibody for HER2-Expressing Cancers



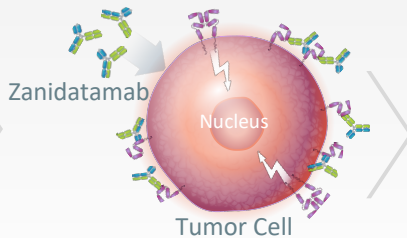
Zanidatamab's unique binding geometry promotes:

- 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
- Inhibition of growth factor-dependent and -independent tumor cell proliferation
- Antibody-dependent cellular cytotoxicity and phagocytosis (ADCC / ADCP); and complement-dependent cytotoxicity (CDC)

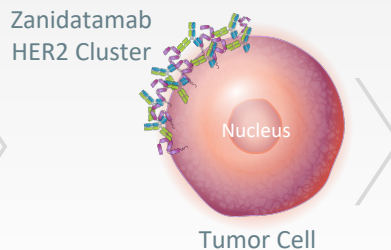
Dual HER2-Binding of Zanidatamab Drives Unique MOA



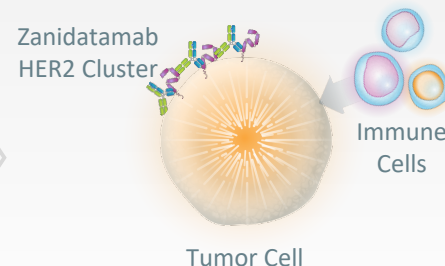
HER2 driven tumor cell emits signals to drive accelerated growth



Zanidatamab arrives to tumor cell and attaches to HER2 proteins



Clusters form on tumor cell, blocking HER2 proteins from emitting signals

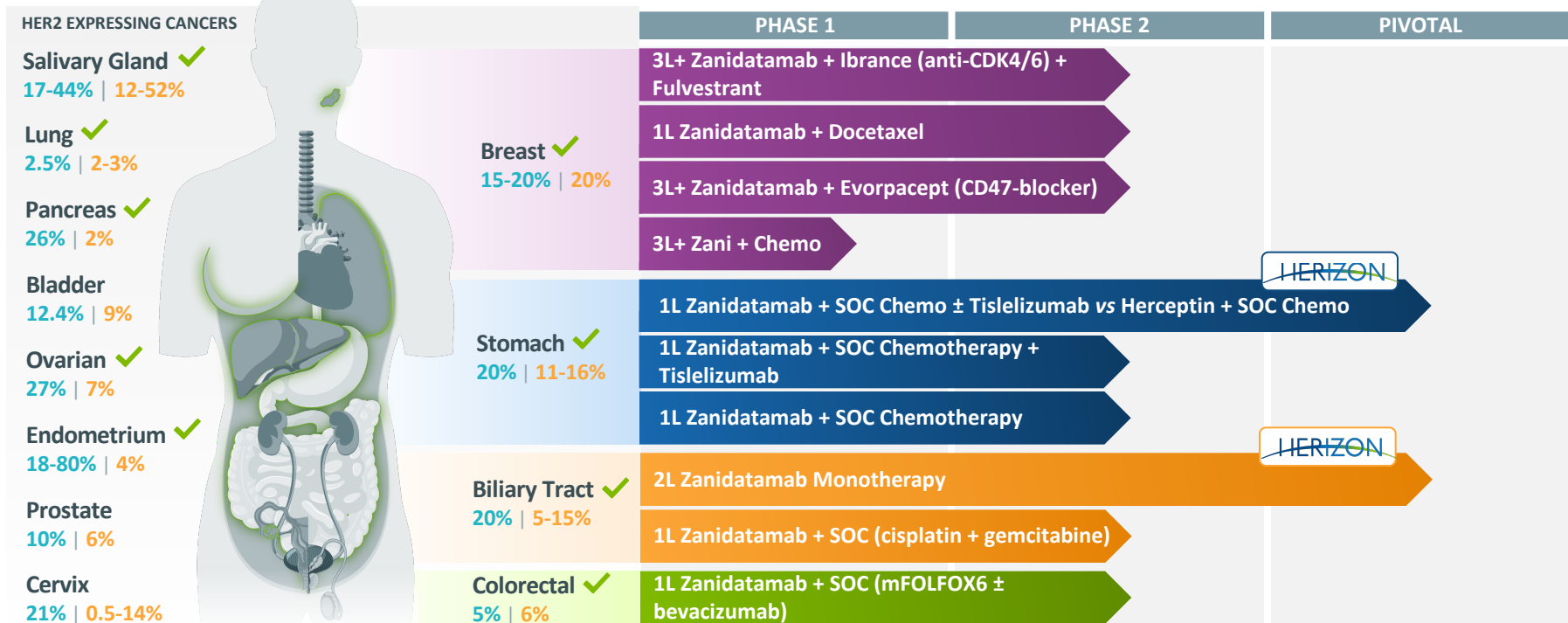


Clusters on tumor cells can attract immune cells to attack and kill the tumor

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.

Broad Opportunity for Zanidatamab in HER2 Cancers

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



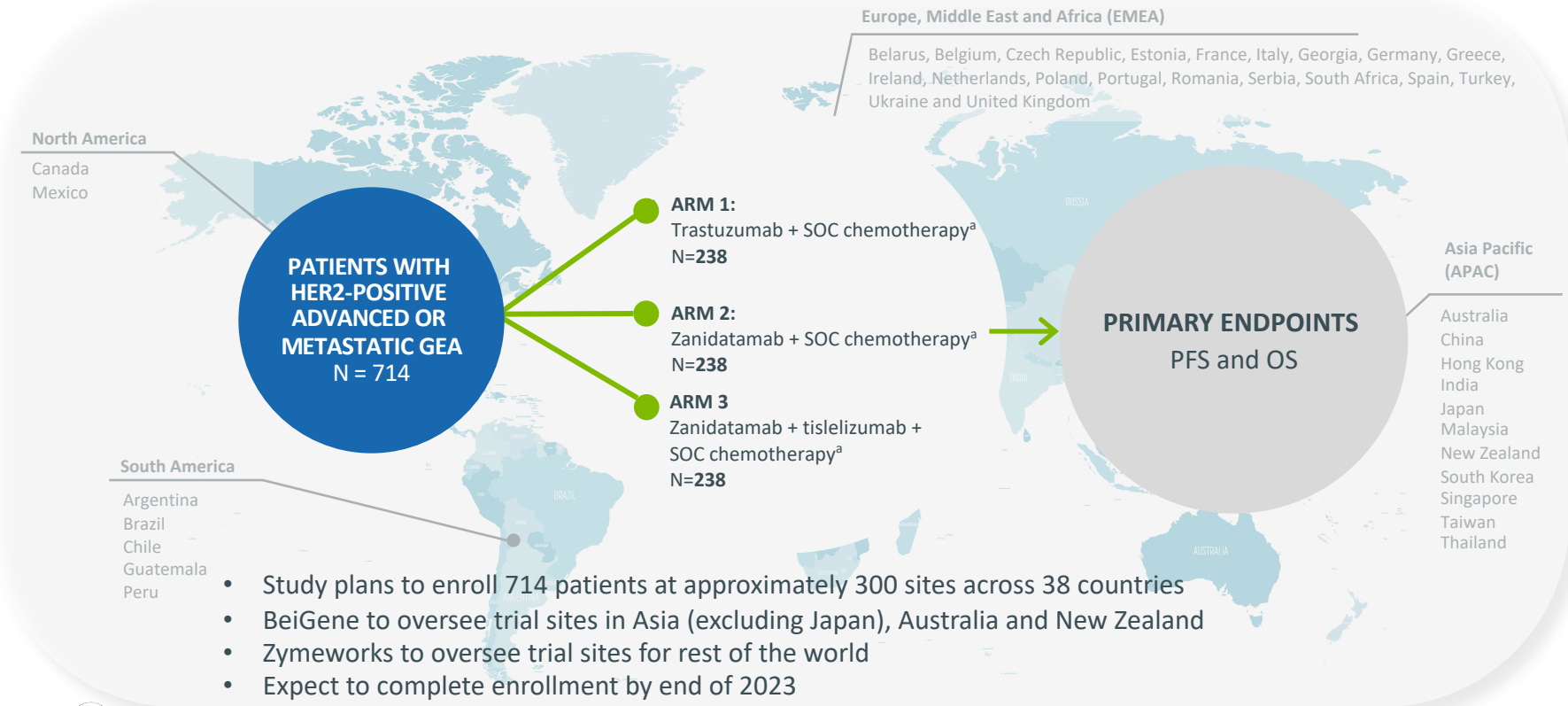
HER2 EXPRESSION | AMPLIFICATION
 ✓ ZANIDATAMAB SINGLE AGENT ACTIVITY

SOC = Standard of Care

HERIZON-GEA-01 Pivotal Study Overview



First-Line HER2-Positive GEA



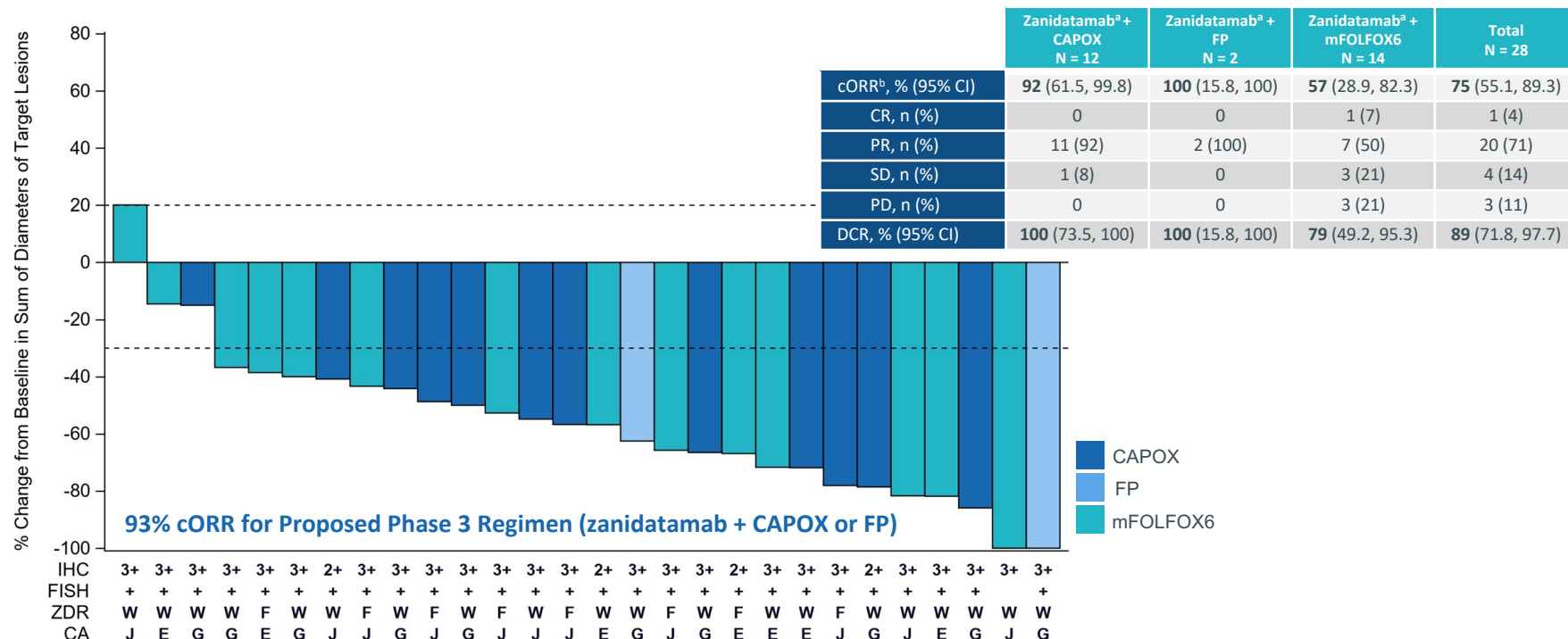
^aSOC (standard of care) chemotherapy: CAPOX or FP

GEA: gastroesophageal adenocarcinoma; PFS: Progression-free survival; OS: overall survival

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.

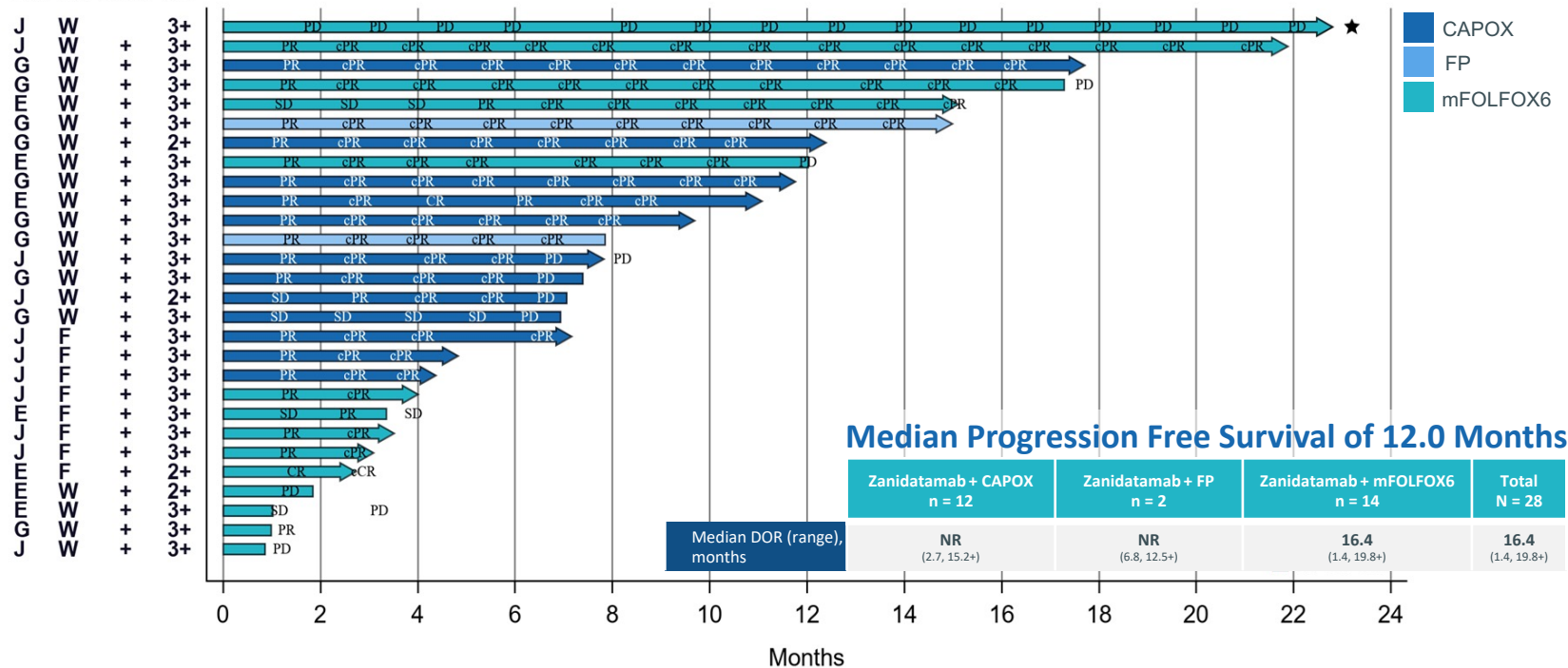
5-FU = 5-fluorouracil; CAPOX = capecitabine plus oxaliplatin; cORR = confirmed objective response rate; CR = complete response; DCR = disease control rate; E = esophageal cancer; F = flat dosing; FISH = fluorescence in situ hybridization; FP = 5-FU and cisplatin; G = gastric cancer; IHC = immunohistochemistry; 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



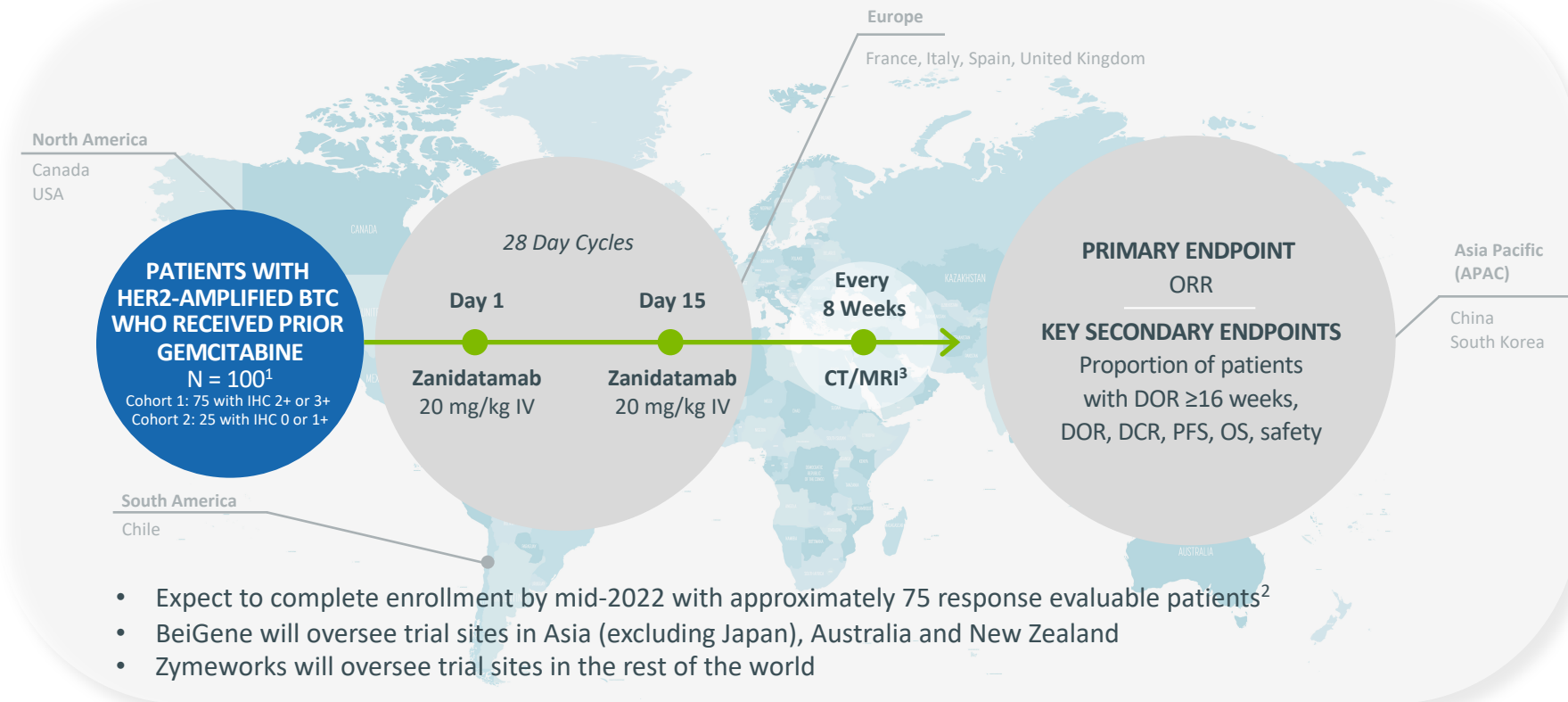
★ An MRI performed for neurologic symptoms on Day 8 demonstrated brain metastases, which were treated with radiation therapy. Subject remained on mFOLFOX6-1 with zanidatamab and has had long term disease control since treatment of brain metastases.

5-FU = 5-fluorouracil; CA, primary tumor location; CAPOX = capecitabine plus oxalipatin; 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 oxalipatin 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.

HERIZON-BTC-01 Pivotal Study Overview



Second-Line HER2-Amplified Biliary Tract Cancer



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.

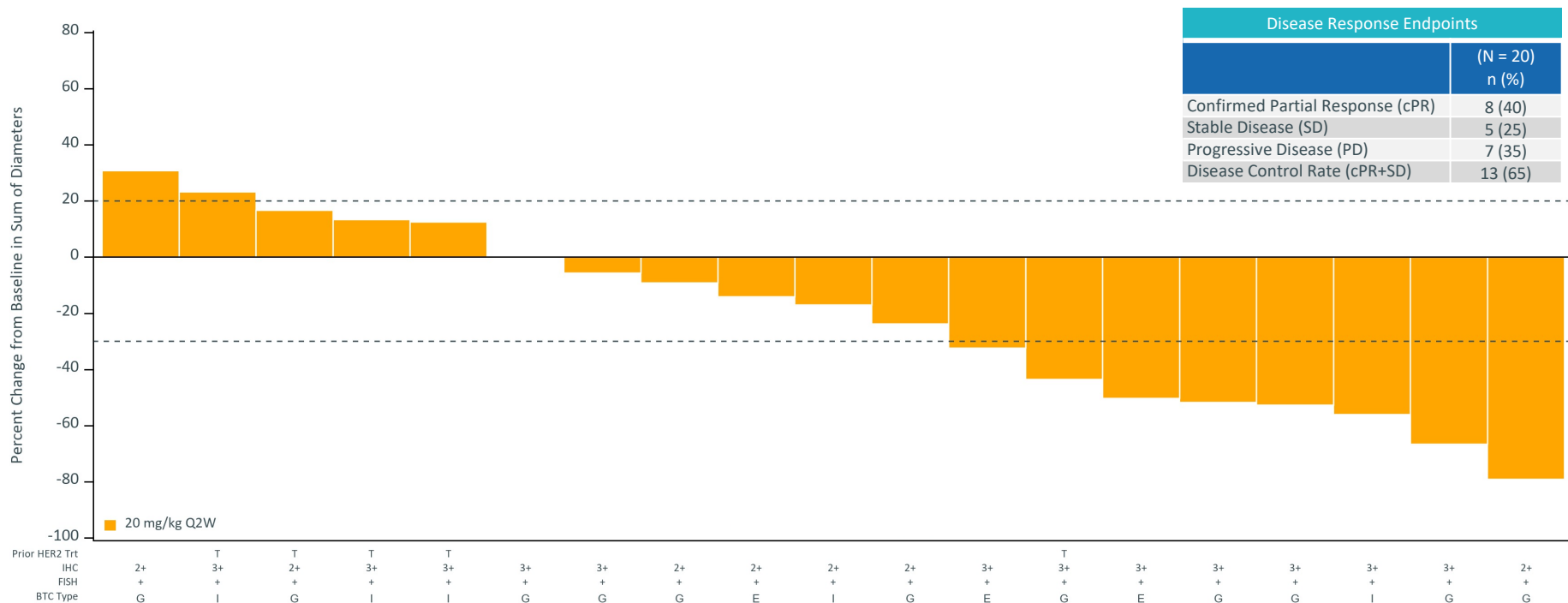
²Complete enrollment for the registration study requires 75 response evaluable patients with HER2 amplification measured as IHC 2+ or 3+.

³For 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



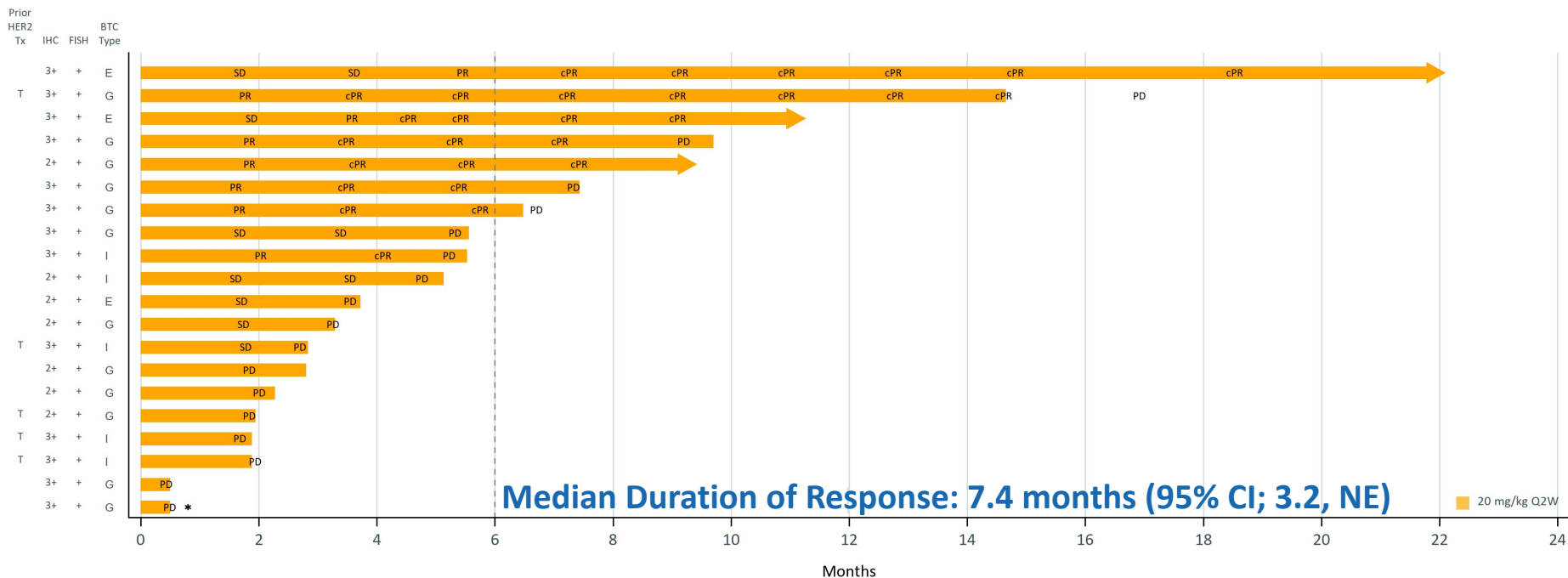
E = Extrahepatic Cholangiocarcinoma; FISH = fluorescence in situ hybridization; I = Intrahepatic Cholangiocarcinoma; IHC = immunohistochemistry; G = Gallbladder; T = trastuzumab; Trt = treatment.
Response-evaluable: all treated patients with measurable disease who had at least one evaluable, post-baseline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

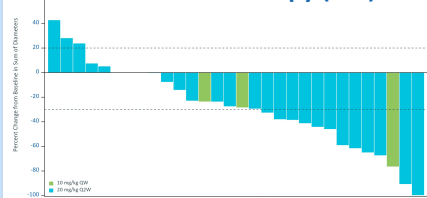
(HERIZON-BTC-01; NCT04466891; Enrollment completion expected mid-2022)



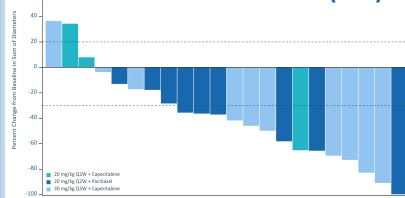
Breadth of Zanidatamab Clinical Data – 3 Key Datasets Expected in 1H 2022

Gastroesophageal

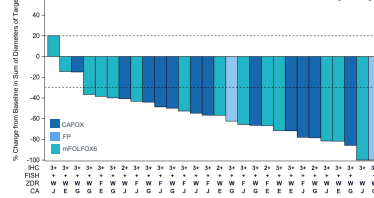
Phase 1 Monotherapy (4L+)



Phase 1 Chemo Combo (3L+)



Phase 2 Chemo Combo (1L)

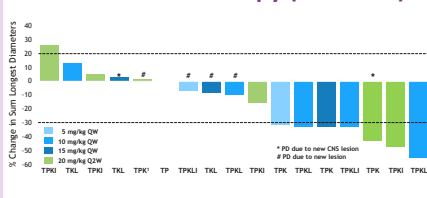


Phase 2 Tisle + Chemo Combo (1L)

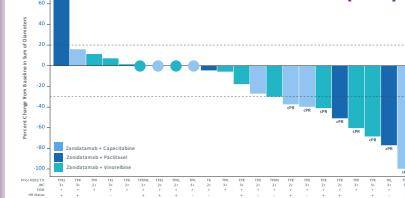
1H 2022

Breast Cancer

Phase 1 Monotherapy (Late-Line)



Phase 1 Chemo Combo (3L+)



Phase 2 CDK4/6 Combo (3L+)

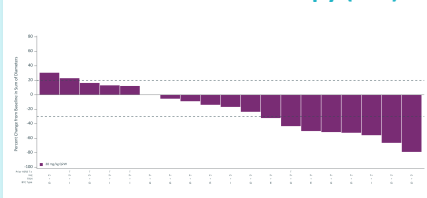
1H 2022

Phase 2 Chemo Combo (1L)

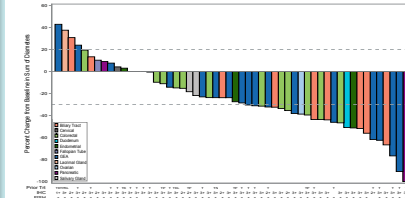
1H 2022

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 \(1L\)](#)

Breast Cancer: [Phase 1 Monotherapy \(Late-Line\)](#), [Phase 1 Chemo Combo \(3L+\)](#)

Other Solid Tumor: [BTC Phase 1 Monotherapy \(2L+\)](#), [Others: Phase 1 Monotherapy \(Late-Line\)](#)

BeiGene Clinical & Commercial Collaboration Overview



Partnership Highlights

- BeiGene has development and commercial rights to zanidatamab and ZW49 in Asia (excluding Japan), Australia and New Zealand
- 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

ZW49: A Bispecific ADC for HER2-Expressing Cancers

Unique Mechanisms of Action

- Biparatopic-induced internalization
- Increased toxin-mediated cytotoxicity
- Enhanced platform tolerability
- Broad therapeutic window
- Potential to address unmet need in high and low HER2-expressing cancers, including brain metastases

Clinical Data Highlights

- Multiple confirmed responses and stable disease observed in several tumor types
- Differentiated safety profile with the majority of adverse events grade 1 or 2, reversible and manageable
- Completed enrollment for expansion cohort targeting 2.5 mg/kg every three weeks
- Weekly dosing regimens continues to progress with a favorable safety profile observed to date

Expected ZW49 Catalysts

- Complete expansion cohorts & define Phase 2 clinical development plan
- Report Phase 1 clinical data at medical meeting in H2 2022



Legacy Partnerships & Collaborations

PROGRAMS PLATFORMS	PRECLINICAL	PHASE 1	PHASE 2	COMMERCIAL RIGHTS
PARTNERSHIPS				
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		
Bispecific Antibody	 	Undisclosed		
Bispecific Antibody	 	Immuno-Oncology		
Bispecific Antibody	 	Infectious Disease/Undisclosed		
Bispecific Antibody	 	Dermatology		
Bispecific Antibody	 	Undisclosed		



Azymetric



EFFECT



Zymeworks

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

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

Active Partnerships with Global Pharmaceutical Leaders

\$225MM+ in Partnership Revenue Received with \$8.5B+ in Total Deal Value



Bispecific Antibody

- Up to 3 programs/assets
- Low-mid single digit royalty
- Total deal value \$891M



Bispecific Antibody

- Development and commercial rights in specific countries for zanidatamab and ZW49; up to 3 additional programs
- Tiered up to 20
- Total deal value \$1.15B



Bispecific Antibody

- Up to 10 programs/assets
- Low-mid single digit royalty
- Total deal value \$1.66B



Bispecific Antibody

- Up to 3 programs/assets
- Low single digit to 10 royalty
- Total deal value \$635M



Bispecific Antibody

- AZYMETRIC: up to 3 programs/assets
- EFFECT: update to 10 programs/assets
- Low-mid single digit royalty
- Total deal value \$2.19B



Bispecific Antibody

- Up to 2 programs/assets
- High single digit-20 royalty
- Total deal value \$480M



**XB002 (ICON-2)
Tissue Factor ADC**

- Solid tumor program
- Mid single digit royalty
- Deal value undisclosed/revenue share



**JNJ-78278343
CD3 x KLK2 Bispecific
JNJ-78306358
CD3 x HLA-G Bispecific**

- Up to 6 programs; 2 are in clinic (solid tumors and castration-resistant prostate cancer)
- Mid single digit royalty
- Total deal value \$1.45B

Key Strategic Priorities for 2022 and 2023

Clinical Programs

- **Fully recruit** HERIZON-BTC-01 and HERIZON-GEA-01 pivotal clinical studies
- **Complete/close out** ongoing early-stage clinical studies for zanidatamab as data become available
- **Communicate** a clear clinical development path for ZW49

Preclinical and R&D

- **Advance** two new antibody-drug conjugate or multispecific product candidates with the goal to submit two Investigational New Drug (IND) applications expected by the end of 2024
- **Support and advance** Zymeworks' core technology platforms and collaborations

Partnering & Finance

- **Execute new partnerships** and collaborations to support development and commercialization of zanidatamab, early-stage R&D pipeline and technology platforms
- **Improve 2022-2023 financial position:** form additional partnerships and collaborations, and monetize existing assets and products

Focused strategic priorities and improved operational performance to deliver exceptional results for patients and our investors



Key Investment Highlights

Near-term market opportunity with zanidatamab in GEA and BTC

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



Bruce Hart, Ph.D.
Senior VP, Regulatory Affairs



Mark Hollywood
Senior VP, Technical
and Manufacturing Operations



Chris Astle, Ph.D.
Senior Vice President
and Chief Financial Officer



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
VP, Legal and Corporate Secretary



Jennifer Kaufman-Shaw, JD
VP, Intellectual Property

