Topline Pivotal Results from HERIZON-BTC-01

Ken Galbraith
Zymeworks Chair & CEO

Neil Josephson, MD
Zymeworks Chief Medical Officer

Shubham Pant, MD MBBS
Professor, Department of Gastrointestinal (GI) Medical Oncology, Division of Cancer Medicine,
The University of Texas MD Anderson Cancer Center, Houston, TX

December 19th, 2022

NASDAQ: ZYME
www.zymeworks.com

Forward-Looking Statement

This presentation and the accompany oral commentary include “forward-looking statements” or information within the meaning of the applicable securities legislation, including Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements in this presentation and the accompanying oral statements include, but are not limited to, statements that relate to the potential of zanidatamab in advanced HER2-expressing cancers with high unmet need; the efficacy, safety and tolerability results from the pivotal Phase 2b HERIZON-BTC-01 clinical trial; the potential therapeutic effects of zanidatamab and our other product candidates; our clinical development of our product candidates and enrollment in clinical trials; anticipated clinical data presentations; expectations regarding future regulatory filings and approvals and the timing thereof; the commercial potential of technology platforms and product candidates; the potential addressable market of zanidatamab; our ability to execute new collaborations and partnerships; the timing and status of ongoing and future studies and the related data; our ability to satisfy potential regulatory and commercial milestones with existing and future partners; and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as “believe”, “expect”, “may”, “anticipate”, “potential”, “pending”, “will”, “would”, “can”, “estimate”, “possible”, “promising” and similar expressions are intended to identify forward-looking statements. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon our current expectations and various assumptions. We believe there is a reasonable basis for our expectations and beliefs, but they are inherently uncertain. 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 various factors, including, without limitation: future clinical trials may not demonstrate safety and efficacy of any of our or our collaborators’ product candidates; promising results from pre-clinical development activities or early clinical trial results may not be replicated in later clinical trials; any of our or our 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 the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations, including impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf, may be more severe and more prolonged than currently anticipated; the impact of new or changing laws and regulations; market conditions; inability to maintain or enter into new partnerships or strategic collaborations; and other factors 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 we undertake 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.

Ken Galbraith

Chair & Chief Executive Officer

Neil Josephson

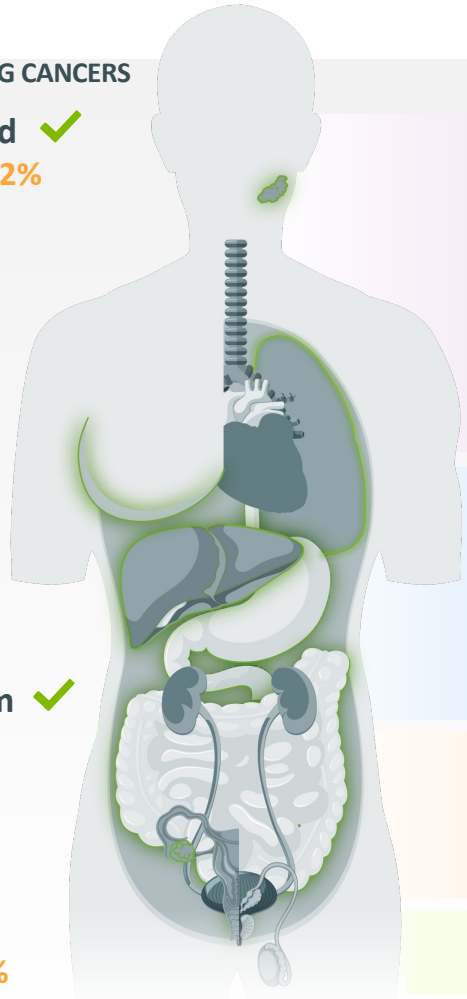
Chief Medical Officer

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 + Palbociclib (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* Trastuzumab + 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

COLLABORATION PARTNERS: BeiGene, Jazz Pharmaceuticals

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

[1] Based on single-agent activity from initial Ph 1 study of zanidatamab as monotherapy

zymeworks

Shubham Pant, M.D. MBBS

Professor, Department of Gastrointestinal (GI) Medical Oncology,
Division of Cancer Medicine, The University of Texas MD
Anderson Cancer Center, Houston, TX

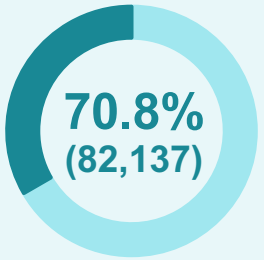
Epidemiology of Biliary Tract Cancers

- Biliary Tract Cancers (BTC) are molecularly diverse tumors which include gallbladder cancer (GBC), intrahepatic cholangiocarcinoma (iCCA), and extrahepatic cholangiocarcinoma (eCCA)[1]

Epidemiology (World)

Incidence varies globally:

- GBC accounts for **0.6%** of all adult cancers **worldwide** (~116,000 new cases in 2020)[2,3]



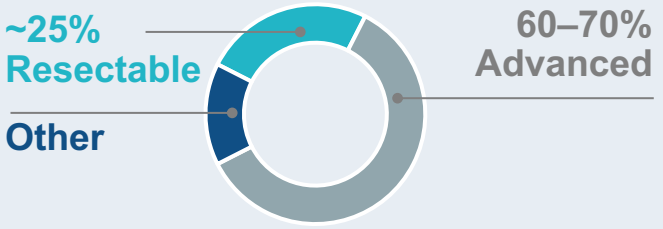
of all estimated new gallbladder cancer cases occurred in Asia in 2020[3]

- 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)[4]
- **~10%** of all estimated new gallbladder cancer cases (12,570) occurred in **Europe in 2020**[3]

Epidemiology (United States)

Most cases are diagnosed at an advanced stage:

CASES BY STAGE AT DIAGNOSIS[5,6]



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

Progression Considerations

Second line:

- 2L chemotherapy yields response rates of less than 10%; median overall survival of patients is often less than 6 months[8] with a recent phase II trial reporting 8.6 months[9]
- ~40-60% of BTC patients present possible targetable alterations with differences between anatomical subgroups[5,10]

19% of GBC
17% of eCCA
5% of iCCA
} **Overexpress HER2[11]**

2L: second line treatment; HER2: human epidermal growth factor receptor 2

1.Bogenberger JM et al., Precision Oncol. 2018; 2.GLOBOCAN. Gallbladder fact sheet. 2020. 3.GlOBOCAN. World fact sheets. 2020; 4.Zhang Y et al., Cancer Epidemiology. 2021; 5.Gómez-España MA, et al., Clin Transl Oncol. 2021; 6.Banales JM et al., Nat Rev Gastroenterol Hepatol. 2020; 7.NCI. SEER. SEER*Explorer: Pancreatic & Biliary Cancer. 2021; 8.Lamarca A et al., J Clin Oncol. 2019; 9.Yoo C et al., Final results (NIFTY) abstract 55P presented at ESMO Congress 2022; 10.Bridgewater JA et al., Am Soc Clin Oncol Educ Book. 2016; 11.Galdy S et al., Cancer Metastasis Rev. 2017

Targeted Treatment Options are Rapidly Evolving in Biliary Tract Cancers

No current 2L standard of care for BTC without FGFR or IDH1 alterations

<table>
<tr><th colspan="3">Unresectable and Metastatic Disease</th></tr>
<tr><th>First-Line Options</th><th>Second-Line Options</th><th>Third-Line</th></tr>
<tr><td rowspan="2">Gemcitabine + Cisplatin ± Durvalumab

TOPAZ-1 Results[1]:
mOS: 12.8 vs 11.5 months
mPFS: 7.2 vs 5.7 months
ORR: 26.7 vs 18.7%</td><td>Chemotherapy
ORR 5-15%[2-3]</td><td rowspan="2">Active Symptom Control</td></tr>
<tr><td>Targeted Therapies*:
FGFR inhibitors: ORR 20-40%[4]
IDH1 inhibitor: ORR 2.4%[5]</td></tr>
<tr><td rowspan="2">Clinical Trial</td><td>Active Symptom Control</td><td rowspan="2">Clinical Trial</td></tr>
<tr><td>Clinical Trial</td></tr>
</table>

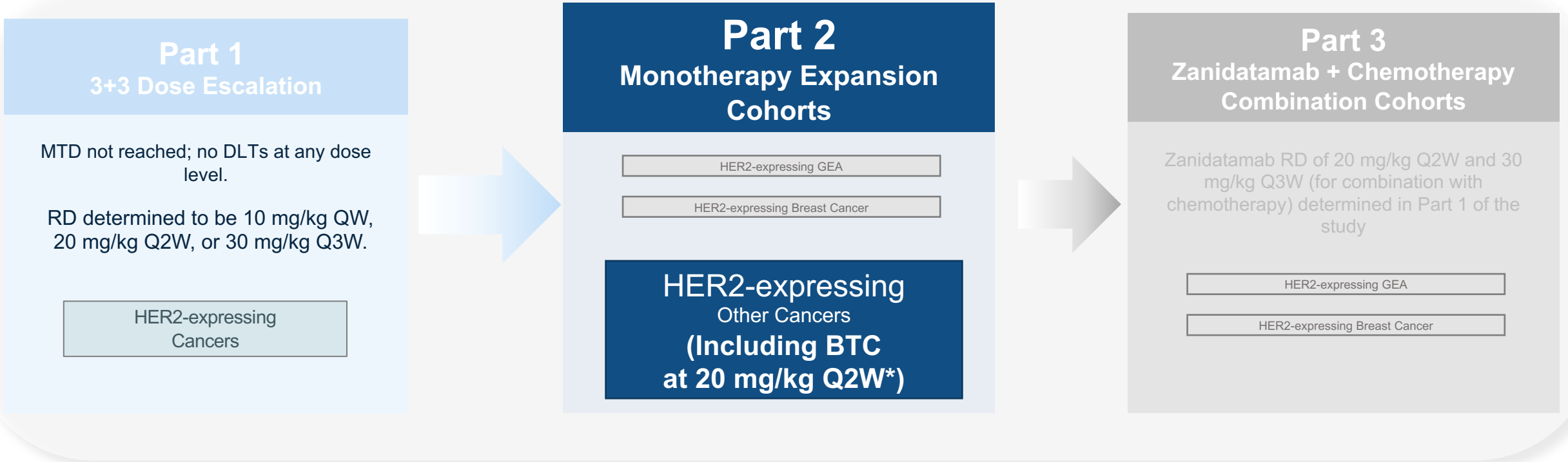
*Actionable driver mutations have been identified and are generally mutually exclusive from one another[6]
ERBB2 (HER2) amplification rates in biliary tract cancer: 2.5-3% iCCA; 8-11% eCCA; 7-16% GBC[7]

2L: second line treatment; eCCA : extrahepatic cholangiocarcinoma; FGFR: fibroblast growth factor receptor; GBC: gallbladder cancer; HER2: human epidermal growth factor receptor 2; iCCA: intrahepatic cholangiocarcinoma; IDH1: isocitrate dehydrogenase 1; ORR: overall response rate

1.Oh D-Y et al., NEJM 2022; 2. Lamarca A et al., J Clin Oncol., 2019; 3. Yoo C et al., J Clin Oncol. 2021; 4. Vogel A et al., on behalf of the ESMO Guidelines Committee. Ann. Oncol 2022; 5. TIBSOVO US PI Aug 2021; 6. Valle JW et al., Lancet 2021; 7. Mirallas O et al., Ann Oncol. 2022

Zanidatamab in Advanced HER2-expressing Cancers: BTC Cohort

Phase 1 multicenter, 3 dose escalation and expansion study to investigate the safety, tolerability, pharmacokinetics and antitumor activity of zanidatamab in patients with locally advanced (unresectable) and/or metastatic HER2-expressing cancers (NCT02892123)



* For Infusion related reactions: prophylaxis with acetaminophen, and antihistamine, and corticosteroid

BTC: biliary tract cancers; DLT: dose limiting toxicities; HER2: human epidermal growth factor receptor 2; GEA: gastric esophageal adenocarcinoma; MTD: maximal tolerated dose; RD: recommended dose; QW: weekly; Q2W: every two weeks; Q3W: every three weeks

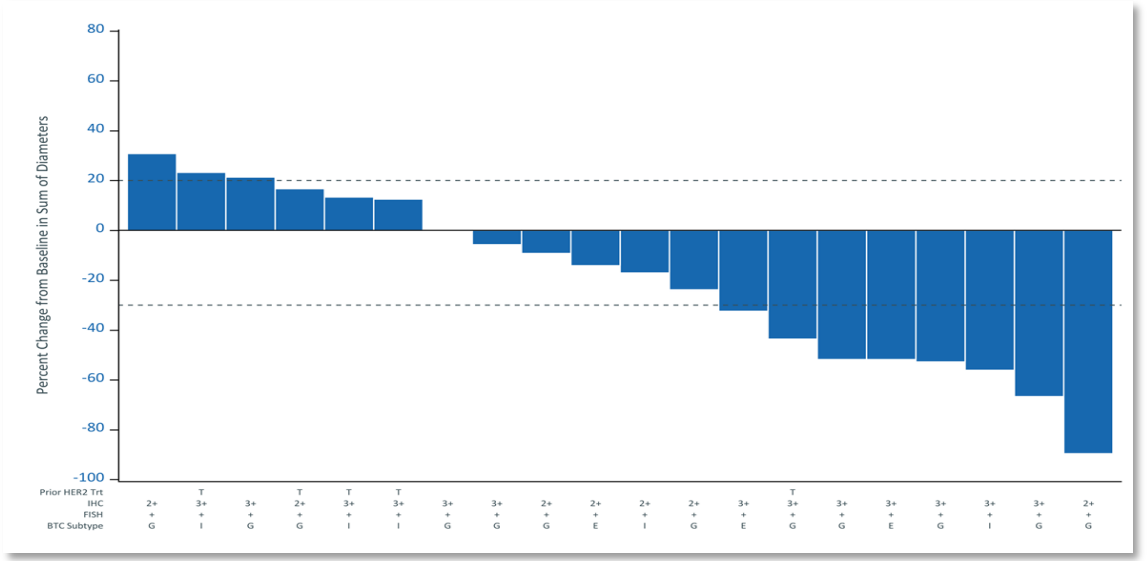
Meric-Bernstam F. Lancet Oncol 2022; published online Nov 15. https://doi.org/10.1016/ S1470-2045(22)00621-0.

Phase 1 Study of Zanidatamab in Advanced HER2-expressing Cancers

- Included 22 patients with previously treated HER2-amplified and expressing BTC:
  - 13 with GBC, 5 with iCCA and 4 with eCCA
- Median 2 prior lines of therapy (including 23% with prior trastuzumab)
- All treated with zanidatamab monotherapy dosed 20 mg/kg Q2W

- Zanidatamab monotherapy was well tolerated and demonstrated promising anti-tumor activity:
  - All treatment-related AEs were Gr 1 -2
  - Confirmed objective response rate of 38.1%
  - Median duration of response of 8.5 months

- Phase 1 data supported:
  - FDA Breakthrough Designation for zanidatamab in previously treated HER2-amplified BTC
  - Development of pivotal trial in 2L HER2-amplified BTC (HERIZON-BTC-01; NCT04466891)



BTC: biliary tract cancers; cPR: confirmed partial response; AE: adverse events; eCCA: extrahepatic cholangiocarcinoma; GBC: gallbladder cancer; Gr: grade; HER2: human epidermal growth factor receptor 2; iCCA: intrahepatic cholangiocarcinoma; PD: progressive disease; Q2W: every two weeks; SD: stable disease; SOD: sum of diameters

Meric-Bernstam F. Lancet Oncol 2022; published online Nov 15. https://doi.org/10.1016/ S1470-2045(22)00621-0.

Conclusions

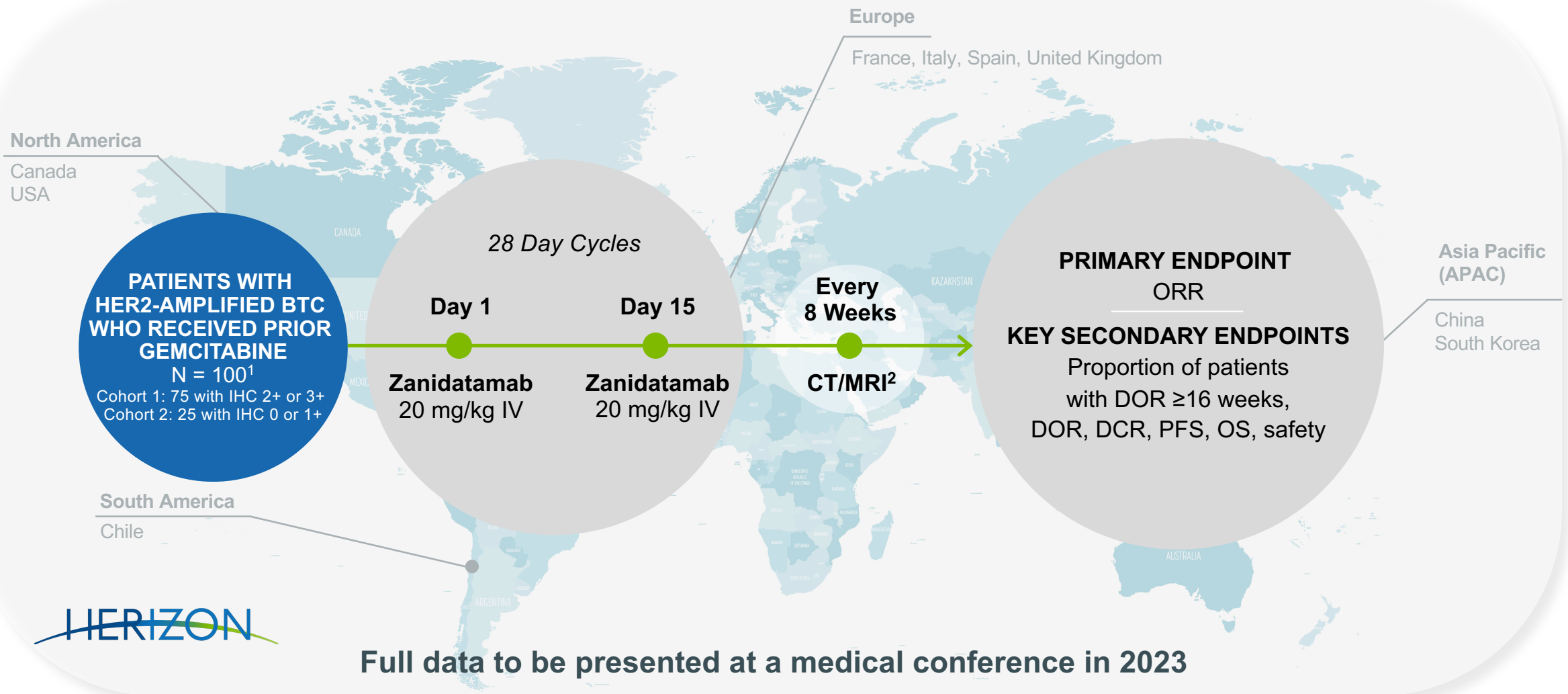
- Zanidatamab monotherapy was well tolerated and demonstrated promising anti-tumor activity in patients with HER2+ BTC that have progressed after prior therapies, including HER2-targeted agents
- All treatment-related AEs were mild or moderate (Grade 1 or 2)
- Disease control rate was 61.9% with a confirmed objective response rate of 38.1% (8/21) and a median duration of response of 8.5 months

Data Supports Pivotal Trial in Second-Line Biliary Tract Cancers
(HERIZON-BTC-01; NCT04466891; Enrollment completed April 2022)

AEs: adverse events; BTC: biliary tract cancers; HER2: human epidermal growth factor receptor 2

Meric-Bernstam F. Lancet Oncol 2022; published online Nov 15. https://doi.org/10.1016/ S1470-2045(22)00621-0.

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



BTC: biliary tract cancers; 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.

Pant S, et al. ASCO.GI. 2021, DOI 10.1200/JCO.2021.39.3_suppl.TPS352

Neil Josephson

Chief Medical Officer

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

Top-Line Results:

- Enrollment completed in April 2022
- N = 80 in primary efficacy cohort of 2L+ BTC patients (GBC, ICC, ECC) with IHC 2+ or 3+; inclusion criteria of at least 1 prior gemcitabine-containing systemic chemotherapy regimen
- Confirmed ORR by independent central review of **41.3%** (95% CI: 30.4, 52.8) compares favorably to standard of care chemotherapy in second-line with historical response rates between 5-15%[1-2]
- Responses were durable, with a median duration of response of **12.9 months** (95% CI: 5.95, NE) as confirmed by independent central review
- Zanidatamab monotherapy exhibited a manageable and acceptable safety profile that was consistent with the previously reported monotherapy experience

Chemo-Free Regimen With Potential to be First HER2-Targeted Therapy Approved for Biliary Tract Cancer Patients Pending FDA Review and Approval

BTC: biliary tract cancer; ECC: extrahepatic cholangiocarcinoma; GBC: gallbladder cancer; ICC: intrahepatic cholangiocarcinoma; IHC: immunohistochemistry; NE: not evaluable; ORR: objective response rate

1.Lamarca A et al., J Clin Oncol. 2019; 2. Yoo C et al., J Clin Oncol. 2021

zymeworks

Acknowledgements

We sincerely thank all patients and their families.

We would also like to thank all the investigators, clinical trial researchers, personnel and staff who contributed to the trial in any way,

as well as Dr. Michael Press and Ms. Ivonne Villalobos at USC Medical Center Pathology Lab for support of HER2 testing.

ZW25-101 study is sponsored by Zymeworks
HERIZON-BTC-01 study is sponsored by Zymeworks and BeiGene, Ltd.

Ken Galbraith

Chair & Chief Executive Officer

Next Steps for Zanidatamab

Next Steps:

- Hold discussions with collaboration partners: JAZZ and BGNE
- Regulatory consultations in USA and relevant foreign jurisdictions in conjunction with partners
- Submission of full HERIZON-BTC-01 results for presentation at a major medical meeting in 2023
- Continue enrollment of front-line Phase 2 BTC clinical trial[1] evaluating zanidatamab in combination with gemcitabine/cisplatin
- Upcoming presentation on January 19th, 2023 at ASCO-GI of our Phase 2 clinical trial[1] evaluating zanidatamab in combination with chemotherapy as first-line treatment for HER2-positive GEA
- Complete global commercial supply arrangements for zanidatamab

ASCO-GI: American Society of Clinical Oncology Gastrointestinal Cancers Symposium; BTC: biliary tract cancer; GEA: gastroesophageal adenocarcinoma

[1] ClinicalTrials.gov Identifier: NCT03929666

Q&A

Ken Galbraith
Zymeworks Chair & CEO

Neil Josephson, MD
Zymeworks Chief Medical Officer

Shubham Pant, MD MBBS
Professor, Department of Gastrointestinal (GI) Medical Oncology, Division of Cancer Medicine,
The University of Texas MD Anderson Cancer Center, Houston, TX