ESMO 2022 Investor & Analyst Webcast

September 12th
4:30pm ET

NYSE: ZYME
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 in this presentation include, but are not limited to, statements that relate to the potential therapeutic effects of zanidatamab, zanidatamab zovodotin and Zymeworks’ other product candidates; Zymeworks’ clinical development of its product candidates and enrollment in its clinical trials; anticipated clinical data presentations; Zymeworks’ 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 “anticipate,” “plan,” “expectation,” “intend,” “may,” “will,” “could,” “can,” “potential,” 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.

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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.

Opening Remarks

Kenneth Galbraith

Chair & CEO

Zymeworks' Product Candidate Pipeline

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

*BeiGene to develop and commercialize in Asia Pacific countries including China, South Korea, Australia, and New Zealand but excluding Japan.
ADC: antibody-drug conjugate; HER2: human epidermal growth factor receptor 2; OVCA: ovarian cancer; TOPO1i: topoisomerase inhibitor

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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 20th, 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 optimizing patient outcomes
- **Advance enrollment** of existing zanidatamab pivotal trials and identify future development paths for zanidatamab and zanidatamab zovodotin (ZW49)
- **Aggressively pursue** and **drive value** through partnerships and collaborations
- **Continually improve financial position** through non-dilutive funding sources

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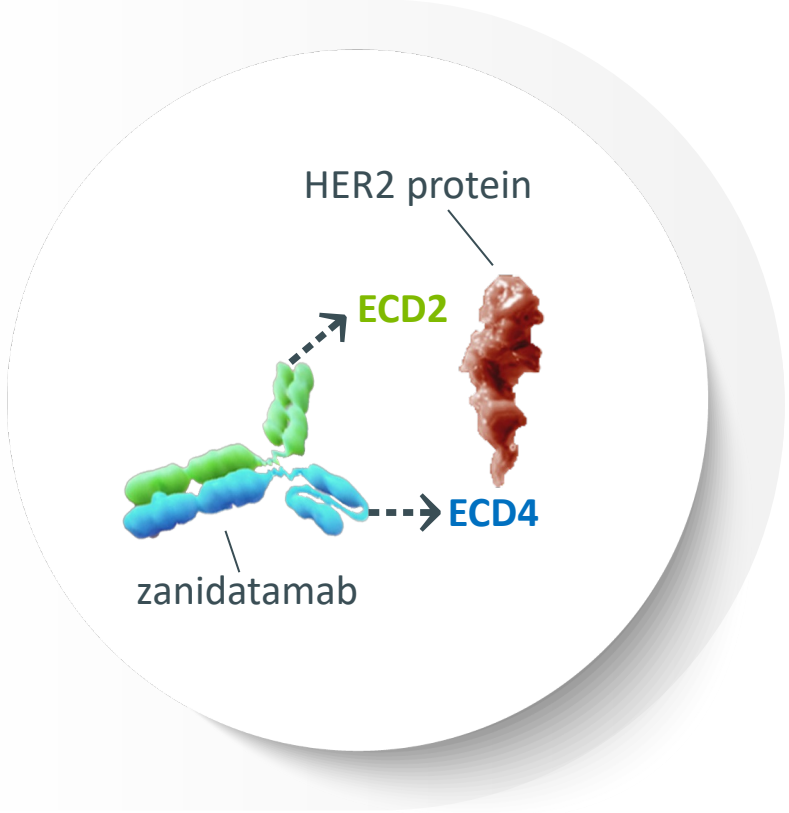
Zanidatamab Zovodotin (ZW49): Background Information & Mechanism of Action

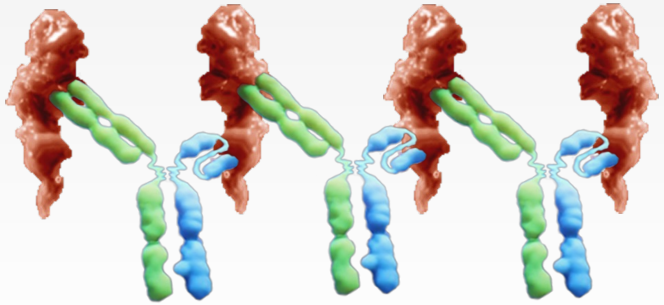
Neil Josephson, MD
Chief Medical Officer

Zanidatamab Zovodotin: HER2-Targeted ADC Built on Zanidatamab Backbone

Zanidatamab MOA



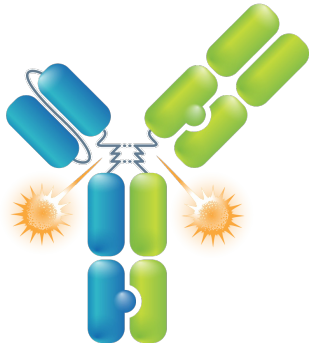
Dual HER2-Binding of Zanidatamab Drives Unique MOA



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

- Biparatopic – targets two distinct HER2 epitopes resulting in HER2 binding across a range of expression levels (low to high)
- More rapid and complete internalization compared to a monospecific ADC
- Delivers a potent cytotoxic agent to targeted cells
- Complete tumor regressions observed in a range of HER2-expressing breast cancer xenograft models
- Expanded therapeutic window demonstrated in non-human primate and mouse models

Zanidatamab Zovodotin



MOA: mechanism of action
Hamblett et al., #3914 Poster Presentation at AACR 2018

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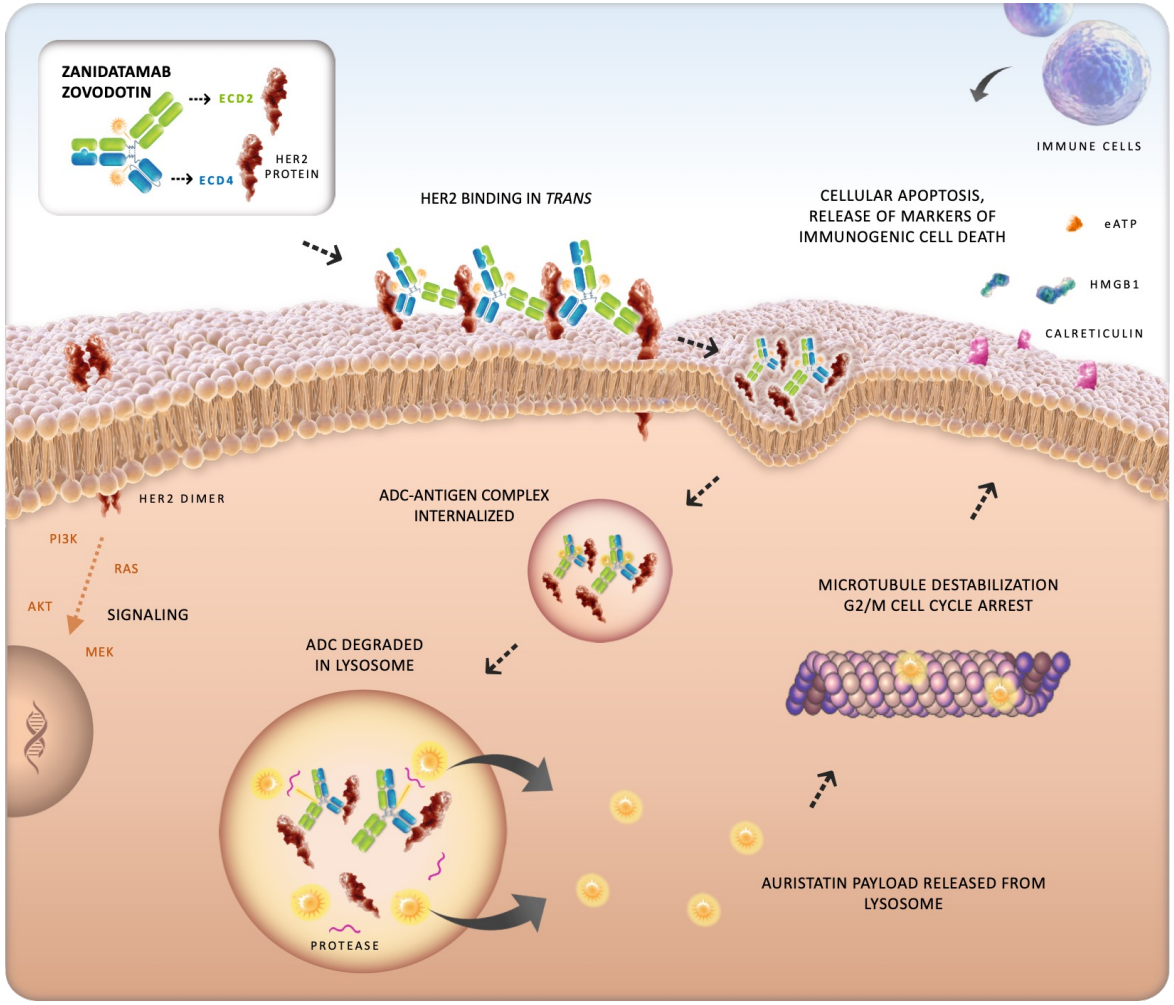
Zanidatamab Zovodotin: A Biparatopic ADC for HER2-Targeted Therapy

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

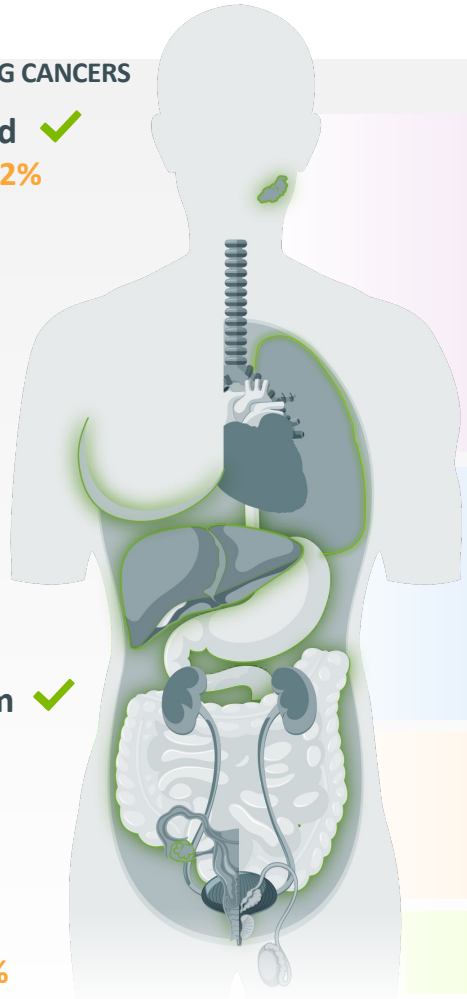
1. Hamblett et al., #3914 Poster Presentation at AACR 2018; 2. Davies et al., #3912, Poster Presentation at AACR 2018; 3. Data on file

Broad Opportunities for 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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Zanidatamab Zovodotin: Development Timeline

Zanidatamab Zovodotin Preclinical and Clinical Timelines

2016

- Strategic partnership and merger agreement with Kairos to acquire Zymelink

2018

- First preclinical data presentation at AACR
- IND submitted to FDA

2019

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

2022

- Phase 1 clinical study results presented at ESMO Annual Congress

IND: investigational new drug application

Preliminary Results From a Phase 1 Study Using the Bispecific, Human Epidermal Growth Factor 2 (HER2)-targeting Antibody-drug Conjugate (ADC) Zanidatamab Zovodotin (ZW49) in Solid Cancers

Komal Jhaveri, MD, FACP

Komal Jhaveri, MD, FACP
Medical Oncologist and Principal Investigator, Memorial Sloan Kettering Cancer Center

Declaration of Interests

Komal Jhaveri, MD, FACP

Consultant/Advisory Board:

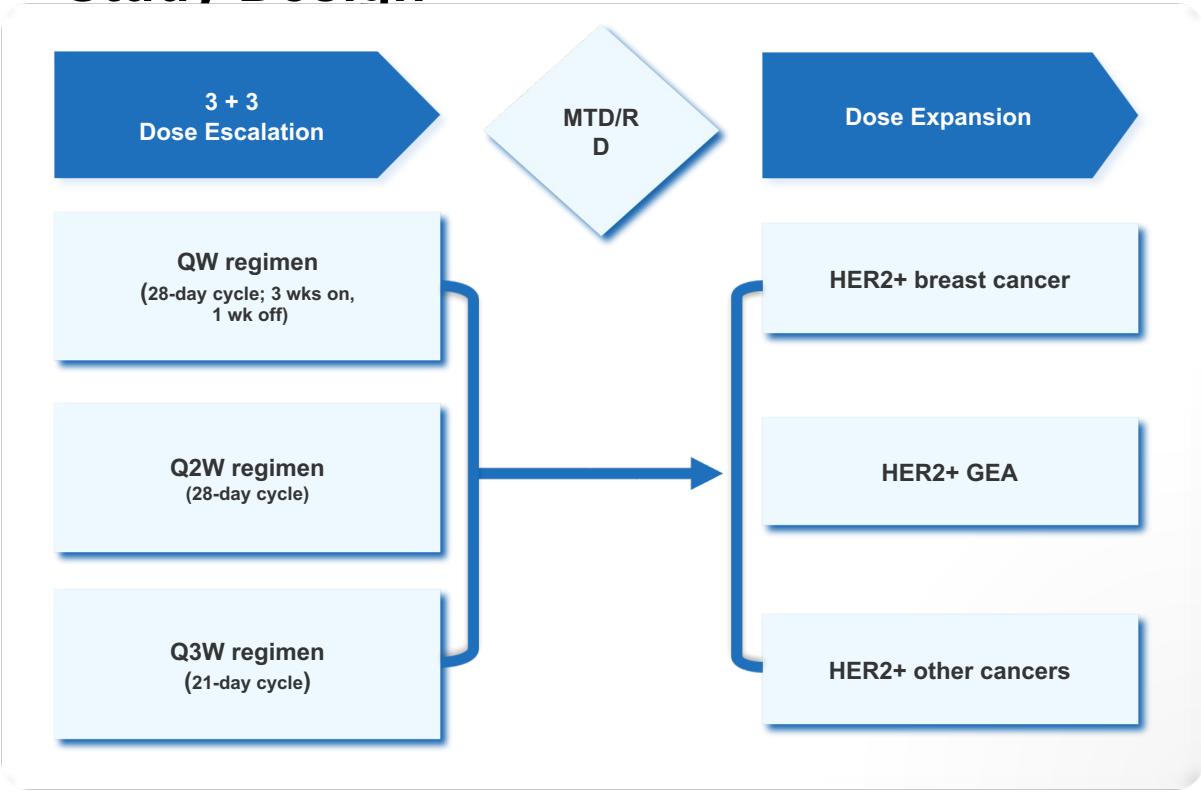
Novartis, Pfizer, BMS, Jounce Therapeutics, Taiho Oncology, Genentech/Roche, AbbVie, Eisai, Astra Zeneca, Blueprint Medicine, Daiichi Sankyo, Seattle Genetics, Lilly/Loxo Oncology, Sun Pharma Advanced Research Company Ltd

Research Funding:

Novartis, Genentech, Astra Zeneca, ADC Therapeutics, Novita Pharmaceuticals, Debio Pharmaceuticals, Pfizer, Lilly Pharmaceuticals, Zymeworks, Gilead, PUMA Biotechnology, Merck Pharmaceuticals

Methods

Study Design



For DE, HER2+ was defined as IHC3+, IHC2+/FISH+ or amplification (+) per FISH or NGS per local testing.
For DX, HER2+ was defined as IHC3+ or IHC2+/FISH+ per central testing.
DE = dose escalation; DX = dose expansion; ECOG = Eastern Cooperative Oncology Group; HER2 = human epidermal growth factor 2; FISH = fluorescence *in situ* hybridization; GEA = gastroesophageal adenocarcinoma; IHC = immunohistochemistry; MTD = maximum tolerated dose; NGS = next-generation sequencing; QW = once every week; Q2W = once every 2 weeks; Q3W = once every 3 weeks; wk = week; RD = recommended dose

Primary Objectives

- To determine the maximum tolerated dose (MTD)/recommended dose (RD) of ZW49
- To characterize the safety and tolerability of ZW49

Secondary Objectives

To evaluate the anti-tumor activity of ZW49 in HER2-expressing cancers

Key Eligibility Criteria

- Refractory HER2-expressing or amplified cancers
  - Patients with HER2+ breast cancer must have received trastuzumab, pertuzumab, and T-DM1
  - Patients with HER2+ GEA must have received trastuzumab
- ECOG performance status 0 or 1

Baseline Disease Characteristics & Disposition

	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)

*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

Data cutoff: 09 Jun 2022

- 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

Treatment-related Adverse Events

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)

* 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

Data cutoff: 09 Jun 2022

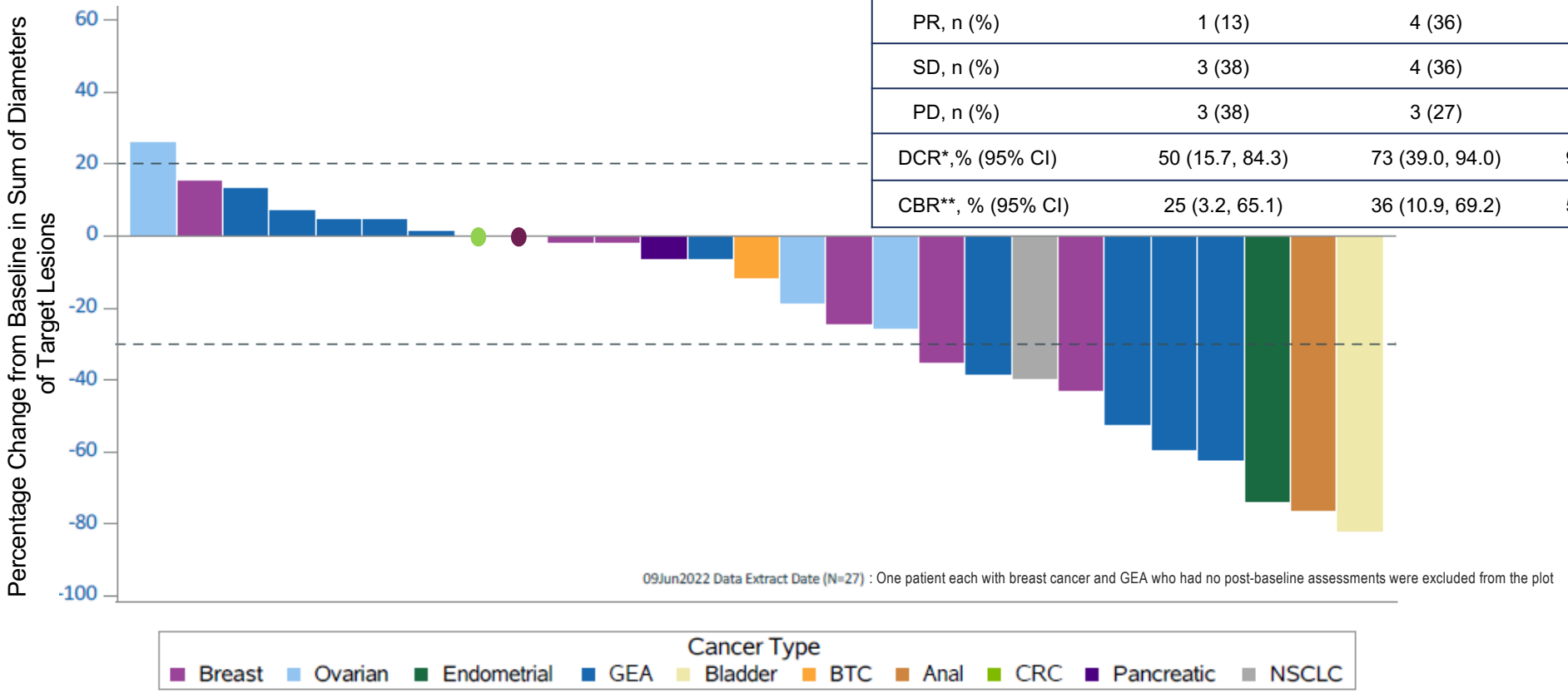
Safety Summary (All Patients)

- 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. Data cutoff: 09 Jun 2022
AE = adverse event; DE= dose escalation; DX = dose expansion; ECG = electrocardiogram; MTD = maximum tolerated dose; Q3W = once every 3 weeks; QT = QT interval

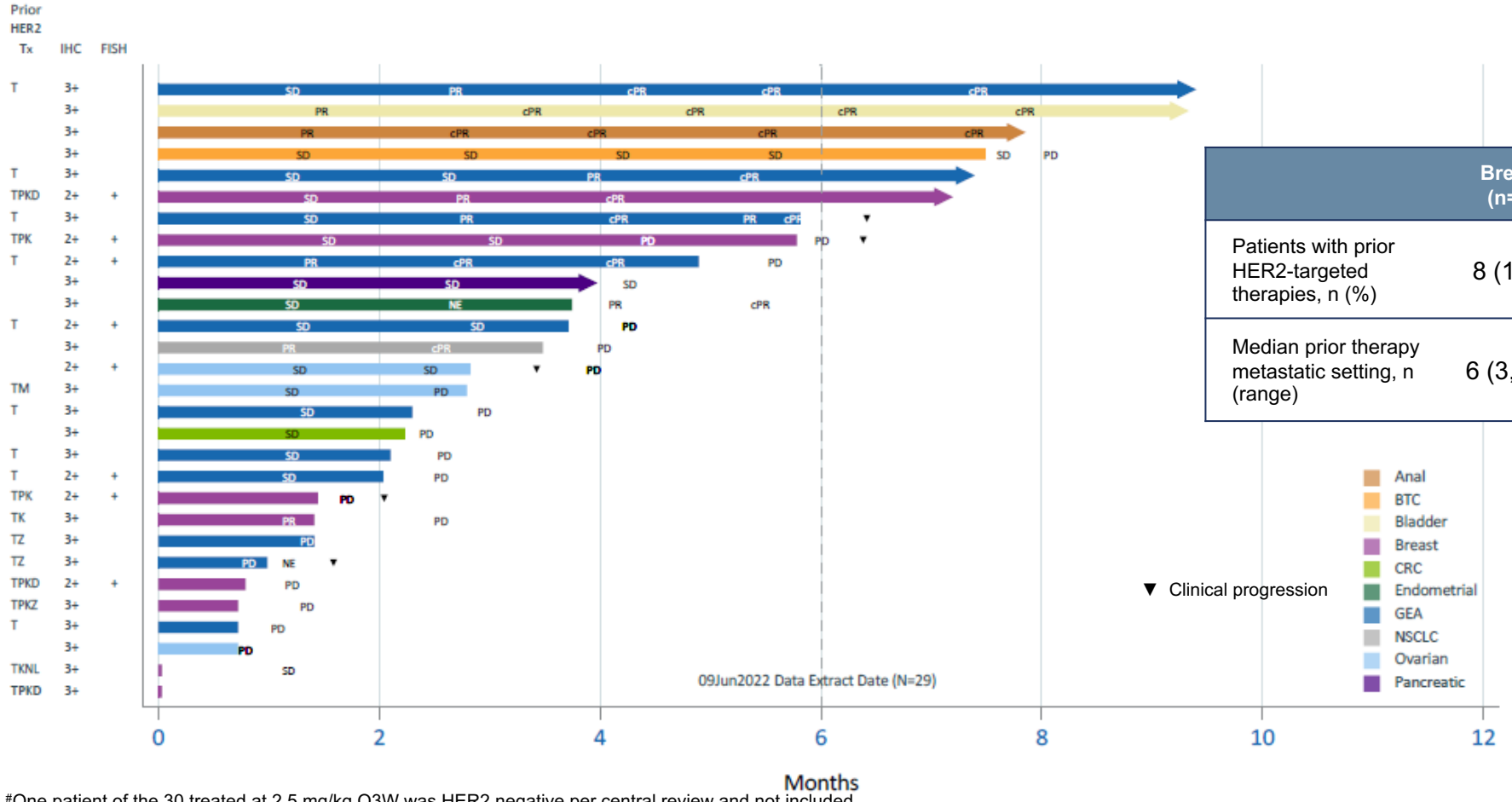
Change in Sum of Target Lesions: Patients with HER2+ Cancers treated with ZW49 at 2.5 mg/kg Q3W (DE + DX)

	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)



#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 = confirmed 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

Treatment Duration: Patients with HER2+ Cancers Treated with ZW49 at 2.5 mg/kg Q3W (DE + DX)



	Breast (n=8)	GEA (n=11)	All 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

Conclusions

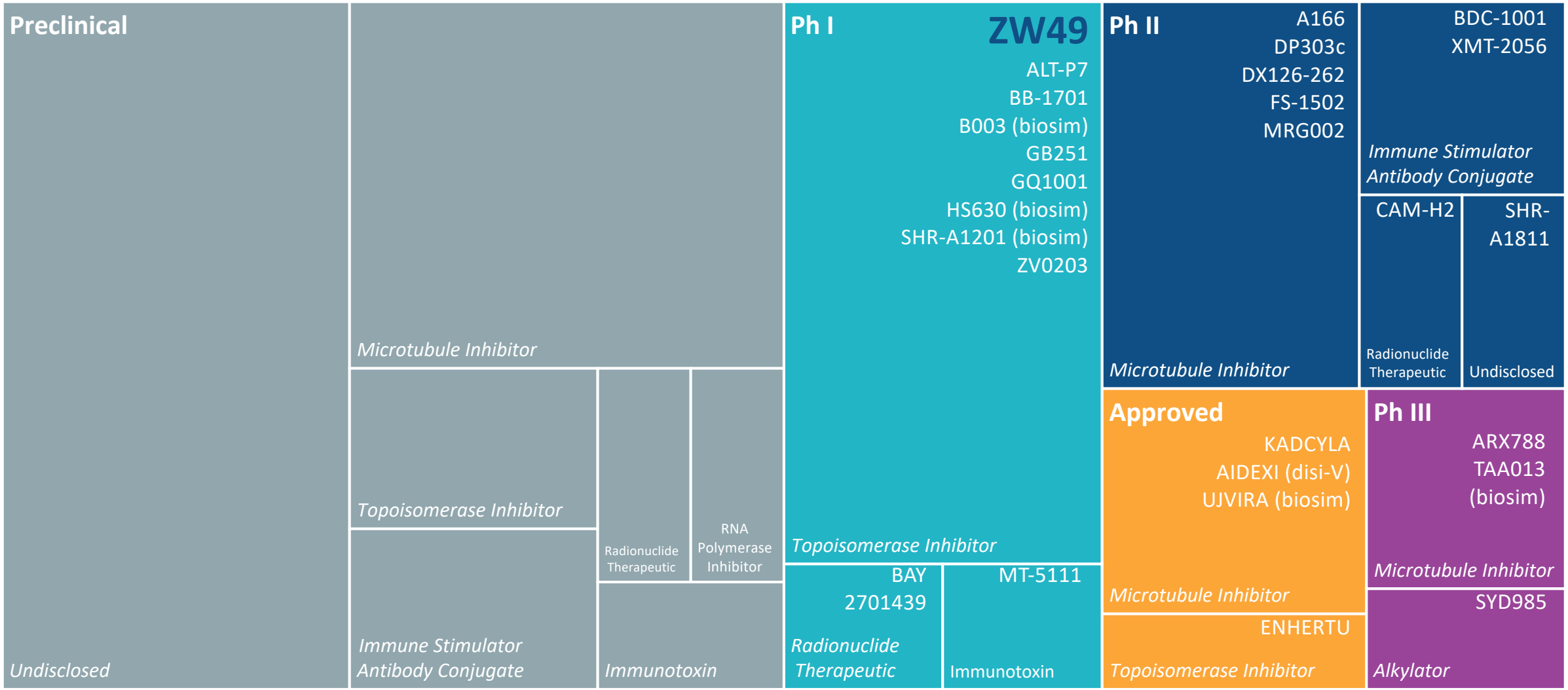
- ZW49 has a manageable safety profile (with the majority of AEs Grade 1 or 2 in severity) and demonstrates encouraging single-agent antitumor activity in heavily pretreated patients with HER2+ solid cancers
- Recommended dose(s)
  - QW is still being evaluated
  - 2.5 mg/kg Q3W

Zanidatamab Zovodotin: A Differentiated HER2-Targeted ADC

Neil Josephson, MD

Chief Medical Officer, Zymeworks

HER2-Targeted ADC Development Landscape (>50 Active Programs)



Note: Programs listed at highest phase of development, internally generated and not exhaustive

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Considerations for Further Development of Zanidatamab Zovodotin

Interim Data in Ongoing Phase 1 study Shows:

- Single-agent activity across multiple HER2-expressing tumor types
- No interstitial lung disease and no significant safety signals for neutropenia or neuropathy
- Keratitis, predominantly grade 1 and 2; reversible and manageable without significant dose discontinuations or delays
- 2.5 mg/kg Q3W dose has activity and tolerability profile to justify further development though we will evaluate full QW data set before establishing the recommended phase 2 dose

Approaches to Further Development:

- Versatile molecule that can be developed as a monotherapy or in combination with standard of care agents
- No overlapping safety concerns for combining with cytotoxic chemotherapy
- Immunogenic cell death has potential synergy with immuno-oncology agents
- Evaluate in diseases that have an unmet need, where there is the potential for combining with established early line standard of care treatments
- Incrementally staged investment in clinical development to preserve and maintain cash runway

Potential Indications for Future Studies

Zanidatamab Zovodotin has shown single-agent activity in multiple tumor types with a differentiated safety profile amongst currently available HER2-targeted ADCs and has multiple avenues 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

Closing Remarks

Kenneth Galbraith

Chair and CEO

Zanidatamab Zovodotin: Path Forward

Acceptable single-agent activity at 2.5 mg/kg every three weeks with weekly dosing still under evaluation

Differentiated safety profile amongst HER2-targeted ADCs allows possibility of **combination with other agents** to improve SOC

Development pathway is clear and with measured investment **will not impact current cash runway guidance**

- Dosing regimen of 2.5 mg/kg q3w shows activity as single agent across multiple indications
  - Continue to study weekly dosing
  - RP2D determination in Q4-22
- Differentiated safety signal amongst ADCs in development
  - Keratitis manageable and reversible, without significant dose interruptions or reductions
  - No interstitial lung disease, pneumonitis, or neutropenia noted to date
- Potential development pathways in NSCLC, mBC, GEA and other indications

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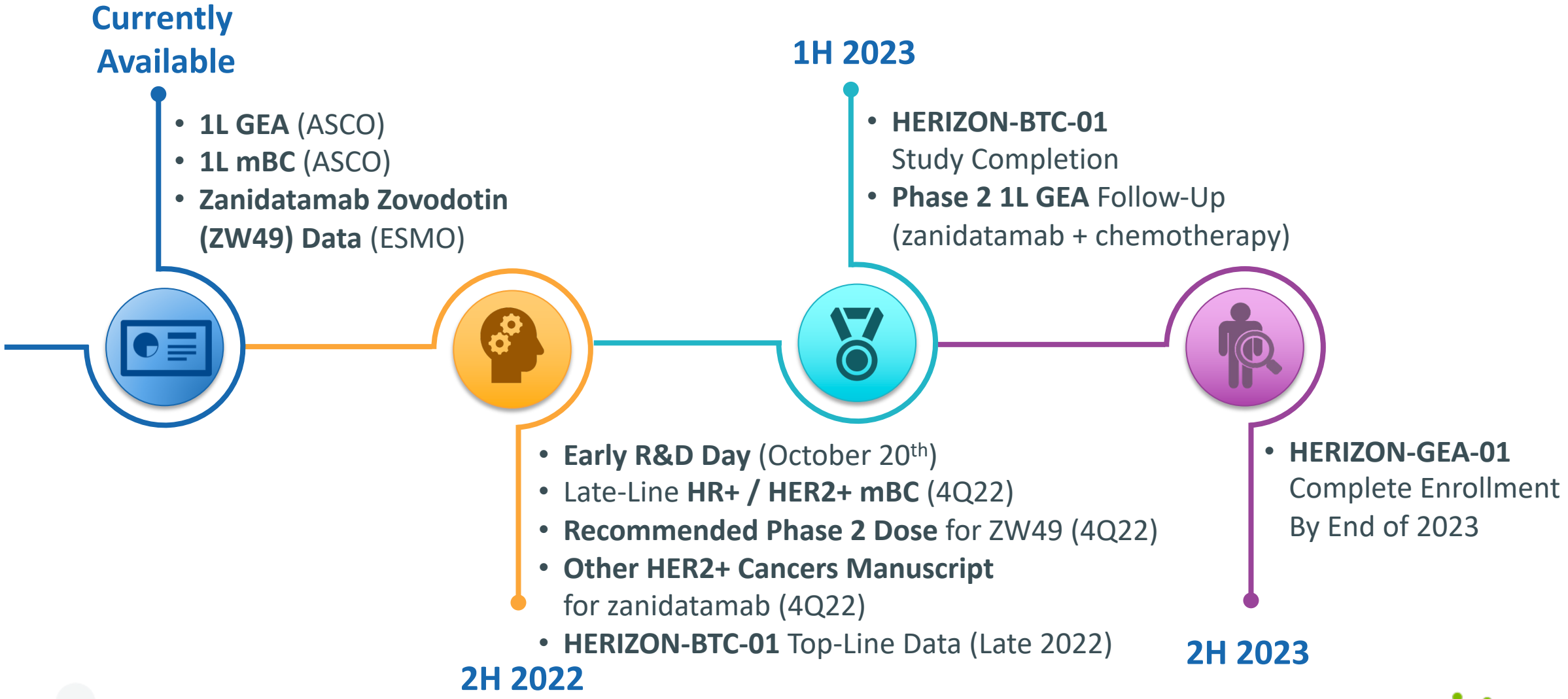
Anticipated Upcoming Data Catalysts



Q&A

Kenneth Galbraith
Chair & CEO

Neil Josephson, MD
CMO

Komal Jhaveri, MD, PHAC
Principal Investigator and Medical Oncologist, Memorial Sloan Kettering Cancer Center