Zanidatamab R&D Day

Differentiated and De-Risked
Caution Concerning Forward-Looking Statements

This presentation contains forward-looking statements and financial targets, including, but not limited to, statements related to: the Company's growth prospects and future financial and operating results, including planned or anticipated clinical trial events, including with respect to initiations, enrollment and data read-outs, and the anticipated timing thereof, and planned or anticipated regulatory submissions and filings; the Company's expectations with respect to its products and product candidates and the potential of the Company's products and product candidates, including expectations with respect to zanidatamab's de-risked, near term opportunity, the potential of zanidatamab to be more than a two billion dollar market opportunity with the potential to raise the standard of care for patients and create long-term value for the Company, and the potential regulatory path related thereto; and other statements that are not historical facts. These forward-looking statements are based on the Company's current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: the successful completion of development and regulatory activities with respect to the Company's product candidates; obtaining and maintaining adequate coverage and reimbursement for the Company's products; the time-consuming and uncertain regulatory approval process, including the risk that the Company's current and/or planned regulatory submissions may not be submitted, accepted or approved by applicable regulatory authorities in a timely manner or at all; the costly and time-consuming pharmaceutical product development and the uncertainty of clinical success, including risks related to failure or delays in successfully initiating or completing clinical trials and assessing patients such as those experienced, and expected to be experienced, by the Company; protecting and enhancing the Company's intellectual property rights and the Company's commercial success being dependent upon its obtaining, maintaining and defending intellectual property protection for its products and product candidates; delays or problems in the supply or manufacture of the Company's products and product candidates; complying with applicable U.S. and non-U.S. regulatory requirements, including those governing the research, development, manufacturing and distribution of controlled substances; government investigations, legal proceedings and other actions; and other risks and uncertainties affecting the Company, including those described from time to time under the caption “Risk Factors” and elsewhere in the Company’s Securities and Exchange Commission filings and reports, including the Company's Annual Report on Form 10-K for the year ended December 31, 2023, and its future filings and reports. Other risks and uncertainties of which the Company is not currently aware may also affect its forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements made in this presentation are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by the Company on its website or otherwise. The Company undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.
Agenda

1. Mechanism of Action
2. Zanidatamab in BTC
3. Zanidatamab in GEA: Dr. Geoffrey Ku
4. Zanidatamab in Breast Cancer
   • Late-Stage: Dr. Sara Hurvitz
   • HER2+/HR+: Dr. Santiago Escrivá-de-Romaní
   • Early-Stage Breast Cancer: Dr. Paula Pohlmann
5. Roadmap to Success
Zanidatamab

Bispecific HER2-Targeted mAb
Zanidatamab is a highly active, differentiated HER2-targeted bispecific mAb with early compelling survival data

- **Novel and Differentiated MOA**
- **Best-in-Class Profile**
  - Addresses Unmet Need
- **Compelling Clinical Data**
  - Supports Fast to Market Strategy
- **$2B+ Commercial Opportunity**

HER2 = human epidermal growth factor receptor 2; mAb = monoclonal antibody; MOA = mechanism of action.
Zanidatamab

Differentiated Leader in the HER2 space
Rob Iannone, M.D., M.S.C.E.

Executive Vice President,
Global Head of Research & Development
Zanidatamab’s Biparatopic Binding Drives Unique MOA and Clinical Activity

- Zanidatamab simultaneously binds two non-overlapping extracellular domains of HER2 (biparatopic binding)

- Unique geometry and binding properties result in multiple mechanisms of action
Zanidatamab’s Biparatopic Binding Drives Unique MOA and Clinical Activity

- Binding properties of zanidatamab are believed to form the foundation of the unique and diverse mechanisms of action observed preclinically and clinically to-date
- Biparatopic binding and engagement of HER2 in trans results in formation of distinct and large HER2 caps / clusters on cell surface
- Trastuzumab (tras), pertuzumab (pert), or the combination of tras + pert were not observed to mediate the formation of HER2 caps, clusters or CDC
Zanidatamab’s Biparatopic Binding Drives Unique MOA and Clinical Activity

- Cap formation is believed to induce better effector activity\(^1\)
- Zanidatamab exhibits strong activation of complement-dependent cytotoxicity (CDC)\(^1\)

\(\text{CDC} = \text{antibody-dependent cellular cytotoxicity; C1q = complement component 1q protein complex; C3a = 77 residue anaphylatoxin; C5a = protein fragment released from cleavage of complement component C5; MOA = mechanism of action; Reference image created with BioRender.com.}^1\)\(\text{Weisser et al. Nat Commun. 2023;14(1):1394.}\)
Zanidatamab Demonstrates Improved Antitumor Activity in Gastric Cancer Xenograft Tumors Compared to Trastuzumab Plus Pertuzumab Combination

Source: Weisser et al. Nat Commun. 2023;14(1):1394. Statistical significance for both models was determined by fitting a linear mixed-effects model on log-transformed tumor growth data and comparing growth rates among all treatment groups, derived from the fitted model. A one-sided F-test is used as an omnibus test on the null hypothesis that all growth rates are equal. A post-hoc two-sided Tukey’s test was used to infer differences in growth rates between treatment groups and account for multiple comparisons. **p < 0.01 vs. trastuzumab or tras + pert. Both datasets are mean ± SEM. CDX = cell line-derived xenograft; IV = intravenous Mg/kg = milligrams per kilogram; PDX = patient-derived xenograft; Pert = pertuzumab; Tras = trastuzumab; zani = zanidatamab.

Mean tumor volume of patient-derived gastric xenograft model GXA 3054 implanted in nude mice. Tumor bearing mice treated with indicated test articles at 30 mg/kg, IV, twice weekly for five weeks, n = 10 per group. ***p value = 3.17e−07

Mean tumor volume of patient-derived gastric xenograft model GXA 3054 implanted in nude mice. Tumor bearing mice treated with indicated test articles at 30 mg/kg, IV, twice weekly for five weeks, n = 10 per group. ***p value = 3.17e−07
Zanidatamab: Recent Data De-Risks Potential Opportunity

Meaningful data generation and rapid progression 15 months post-transaction

Monotherapy Activity
- Positive monotherapy pivotal data1 in previously treated HER2-amplified BTC
- Jazz confirms opt-in

Transaction Announced
- Option to in-license zanidatamab ahead of BTC data

BTC Data Presented at ASCO
- Voted Best of ASCO presentation

Announced MD Anderson Collaboration
Studying zanidatamab as monotherapy and in combination in:
- Early-stage BC
- Cancers where other HER2-targeted therapies failed
- Rare, tissue agnostic cancers

Activity in Combination
- First triplet data presented in 1L GEA at ESMO4
- Zanidatamab + chemotherapy + tislelizumab
- Demonstrated promising activity in combination

Activity Post Prior HER2 Treatment
- Promising late-line mBC data at SABCS shows activity in patients previously treated with HER2-targeted agents5
- Zanidatamab + Palbociclib + Fulvestrant
- Activity in novel chemo-free combination regimen

Monotherapy Activity
- Zanidatamab + chemotherapy doublet data at ASCO G12
- Announced inclusion in I-SPY 2 Trial3

Promising Early OS Data

1L = first line; ASCO = American Society of Clinical Oncology; BC = breast cancer; BTC = biliary tract cancer; ESMO = European Society for Medical Oncology; GEA = gastroesophageal adenocarcinoma; GI = gastrointestinal; HER2 = human epidermal growth factor receptor 2; mBC = metastatic breast cancer; OS = overall survival; SABCS = San Antonio Breast Cancer Symposium; DOI: 10.1200/JCO.2023.41.16_suppl.1044 Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 1044-1044; DOI: 10.1200/JCO.2023.41.4_suppl.347 Journal of Clinical Oncology 41, no. 4, suppl (February 01, 2023) 347-347; NCT01042379, in collaboration with QuantumLeap Healthcare Collaborative; *Poster presented by partner BeiGene; Harpreet Wasan, et al. Zanidatamab (zani) plus chemotherapy (chemo) and tislelizumab (TIS) as first-line (1L) therapy for patients (pts) with advanced HER2-positive (+) Gastric/gastroesophageal junction adenocarcinoma (GC/GEJC); updated results from a phase 1b/2 study, ESMO, 2023; Santiago Escrivá-de-Romani, et al., Primary Results From a Phase 2a Study of Zanidatamab (zani) + Palbociclib (palbo) + Fulvestrant (fulv) in HER2+HR+ Metastatic Breast Cancer (mBC), SABCS, 2023.
Zanidatamab has shown monotherapy activity across a broad range of HER2-expressing tumor types in multiple lines of therapy.

Zanidatamab is Effective in Multiple Combination Therapies

**Zanidatamab combines effectively with multiple agents**

In early- and late-line therapy, combination therapy shows effective antitumor activity.

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**1L GEA: Phase 2 Zanidatamab + Chemotherapy + Tislelizumab**

**1L GEA: Phase 2 Zanidatamab + Chemotherapy**

**1L BC: Phase 2 Zanidatamab + Palbociclib + Fulvestrant**

**1L BC: Phase 2 Zanidatamab + Docetaxel**

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1L = first line; BC = breast cancer; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; Lee et. al., ASCO 2022; Elimova et. al., ASCO GI 2023; Escriva-de-Romani et. al., SABCS 2023; Wang et.al., ASCO 2023.
Zanidatamab has shown activity after treatment with HER2-targeted therapies:

- T-DXd
- T-DM1
- Trastuzumab
- Pertuzumab
- Tucatinib
- Lapatinib
- Neratinib
- Margetuximab

3/4L = third / fourth line; BC = breast cancer; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; T-DM1: trastuzumab emtansine, Kadcyla®; T-DXd = trastuzumab deruxtecan, or Enhertu®; Escriva-de-Romani et. al., SABCS 2023; Meric-Bernstam et. al., ASCO-GI 2021; Bedard et. al., SABCS 2021; Oh et. al, ESMO-Asia 2019.
Zanidatamab has Demonstrated Durable Activity in Multiple Indications

1L GEA: Phase 2 Zanidatamab + Chemo

Late-Line HR+/HER2+ BC: Phase 2 Zanidatamab + Palbociclib + Fulvestrant

1L BC: Phase 2 Zanidatamab + Chemo

2L+ BTC Pivotal: Phase 2 Zanidatamab Monotherapy

1/2L = first / second line; BC = breast cancer; BTC = biliary tract cancer; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor.

1. Pant et. al., ASCO 2023;
2. Escriva-de-Romani et. al., SABCS 2023;
3. Elimova et. al., ASCO GI 2023;

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1/2L = first / second line; BC = breast cancer; BTC = biliary tract cancer; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor.

1. Pant et. al., ASCO 2023; 2. Escriva-de-Romani et. al., SABCS 2023; 3. Elimova et. al., ASCO GI 2023; 4. Wang et. al., ASCO 2023.
Zanidatamab in BTC

Potential to be the First Approved HER2-Targeted Therapy
**Unmet Need in BTC: No Approved HER2-Targeted Therapies**

**ASCO Annual Meeting**
Positive HERIZON-BTC-01 Trial Results

- Oral presentation of top-line BTC data
  Voted Best of ASCO 2023
- Safety profile was consistent with that observed in previous monotherapy studies

- **Initiated BLA submission** in 2L BTC for potential accelerated approval
- **Initiated 1L BTC Confirmatory Trial**

<table>
<thead>
<tr>
<th></th>
<th>cORR</th>
<th>mDOR</th>
<th>mPFS</th>
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<tbody>
<tr>
<td>Zanidatamab</td>
<td>41.3%</td>
<td>12.9m</td>
<td>5.5m</td>
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<tr>
<td>DESTINY-PanTumour02 (T-DXd)</td>
<td>22%</td>
<td>8.6m</td>
<td>4.6m</td>
</tr>
<tr>
<td>MyPathway (Trastuzumab + Pertuzumab)</td>
<td>23%</td>
<td>10.8m</td>
<td>4.0m</td>
</tr>
<tr>
<td>ABC-06 (mFOLFOX)</td>
<td>5%</td>
<td>NR</td>
<td>4.0m</td>
</tr>
</tbody>
</table>

**DESTINY-PanTumor02 (T-DXd)**
MyPathway (Trastuzumab + Pertuzumab)
ABC-06 (mFOLFOX)

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ASCO = American Society of Clinical Oncology; BTC = biliary tract cancer; BLA = biologics license application; cORR = confirmed overall response rate; mDOR = median duration of response; mPFS = median progression-free survival; NR = not reported; T-DXd = trastuzumab deruxtecan, or Enhertu®. 
BTC Represents a Significant Unmet Need

BTC = biliary tract cancer; HER2 = human epidermal growth factor receptor 2; HER2+ = IHC3+ or IHC2+/ISH+; IHC = immunohistochemistry.

1 BTC overall diagnosed patients as per SEER 22; 2 Assumes anatomic subsites intrahepatic CCA, extrahepatic CCA, gallbladder cancer, and BTC unspecified; 3 Assumes HER2 positivity rates per anatomical subsite from: Galdy, S., Lamarca, A., McNamara, M.G. et al. Cancer Metastasis Rev 6, 141–157 (2017), Nobuyoshi Hiraoka, et al. Human Pathology, Volume 105, 2020, Pages 9-19; 4 Major markets: U.K, France, Germany, Spain, Italy. Note: HER2+ BTC patients in Jazz controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd

BTC opportunity of
~12,000 cases annually\(^2\)
in U.S., Europe\(^4\) and Japan

~3,000
HER2+ BTC patients annually\(^1-3\)
Zanidatamab Development Timeline in BTC

2024

- ✔ Initiated confirmatory trial in 1L BTC
- ✔ Complete rolling BLA submission in 2L BTC
- ☐ Expect overall survival data from HERIZON-BTC-01
- ☐ Potential guideline and compendia listing

2025+

- ☐ Potential launch in 2025, or earlier, dependent upon FDA review
- ☐ Commercial launch ex-U.S.
- ☐ Complete 1L BTC confirmatory trial
De-Risked Expansion Opportunity in 1L BTC

Key Inclusion Criteria:
- BTC: GBC, ICC, ECC
- HER2-positivity
  - IHC 3+ or IHC 2+/ISH+
- No PD-1/PD-L1 expression required
- No prior treatment in the locally advanced or metastatic setting

Primary Endpoint:
- PFS (IHC3+)

Secondary / Exploratory Endpoints:
- PFS (allcomers)
- OS
- ORR
- DOR
- Safety
- HEOR/QOL
- Biomarkers

1:1 Randomization
N = 286

Zanidatamab + Gem/Cis +/- PD-1/PD-L1 Inhibitor

Gem/Cis +/- PD-1/PD-L1 Inhibitor

Note: PD-L1 inhibitor use is determined by regional standard of care. BTC = biliary tract cancer; DOR = duration of response; ECC = extrahepatic cholangiocarcinoma; HEOR/QOL = health economics and outcomes research / quality of life; ICC = intrahepatic cholangiocarcinoma; IHC3+ = immunohistochemistry 3+; GBC = gallbladder cancer; ORR = objective response rate; OS = overall survival; PD-1/PD-L1 = programmed cell death protein 1 / programmed cell death ligand 1.
Zanidatamab in GEA
Geoffrey Ku, M.D.

Head of Esophagogastric Section on the Gastrointestinal Oncology Service
Memorial Sloan Kettering Cancer Center Department of Medicine
Gastric and esophageal adenocarcinoma

**Resectable**
- Neoadjuvant therapy
  - Chemo
  - Chemo + Radiation
- Surgery
- Adjuvant therapy
  - Chemo
  - Chemo + Radiation
  - Nivolumab

**HER2+ Unresectable, locally advanced / metastatic GEA**
- **HER2+ 1L Unresectable**
  - PD-L1+
  - Trastuzumab + pembrolizumab + chemo (KEYNOTE-811)
  - Zanidatamab ± tislelizumab + chemo (HERIZON-GEA-01)
- **PD-L1-**
  - Trastuzumab + chemo
  - Zanidatamab + chemo (HERIZON-GEA-01)

**HER2+ 2L Unresectable**
- **PD-L1+**
- T-DXd

Key ongoing Jazz trials
- Keytruda awaiting full approval in EU5/Japan; Japan uses different chemo regimen from U.S.

Source: NCCN Guidelines. 1L = first line; EU5: Major EU markets, U.K, France, Germany, Spain, Italy; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; PD-L1 = programmed cell death protein 1; T-DXd = trastuzumab deruxtecan, or Enhertu®.
**GEA Treatment Paradigm Highlights Unmet Need**

### Gastric and esophageal adenocarcinoma

**Resectable**
- Neoadjuvant therapy
  - Chemo
  - Chemo + Radiation
- Surgery
  - Adjuvant therapy
  - Chemo
  - Chemo + Radiation
  - Nivolumab

**Current resectable treatment pathway does not differ on HER2 status**

**HER2+ Unresectable, locally advanced / metastatic GEA**

**HER2+ 1L Unresectable**
- PD-L1+
  - Trastuzumab + pembrolizumab + chemo (KEYNOTE-811)
- PD-L1-
  - Zanidatamab ± tislelizumab + chemo (HERIZON-GEA-01)

**HER2+ 2L Unresectable**
- T-DXd

**HER2-**
- Trastuzumab + chemo
- Zanidatamab + chemo (ASCO GI)

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**Source:** NCCN Guidelines. 1L = first line; ASCO GI = American Society of Clinical Oncology Gastrointestinal; EU5: Major EU markets, U.K., France, Germany, Spain, Italy; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; PD-L1 = programmed cell death protein 1; T-DXd = trastuzumab deruxtecan, or Enhertu®.

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**Key ongoing Jazz trials**

**Zanidatamab + chemo (ASCO GI)**

**Keytruda awaiting full approval in EU5/Japan; Japan uses different chemo regimen from U.S.**
Zanidatamab + Chemo in 1L GEA: Observed Clinical Activity and Benchmarks

**cORR**
- Zanidatamab + Chemo: 79%
- KN-811: 73%
- TOGA: 47% – 60%

**mDOR**
- Zanidatamab + Tislelizumab + Chemo: 20.4m
- Zanidatamab + Chemo: 11.3m – 6.9m
- KN-811: 11.3m – 6.9m
- TOGA: 12.5m

**mPFS**
- Zanidatamab + Tislelizumab + Chemo: 12.5m
- Zanidatamab + Chemo: 10.0m – 6.7m
- KN-811: 12.5m – 8.1m
- TOGA: 12.5m – 8.1m

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1L = first line; cORR = confirmed objective response rate; GEA = gastroesophageal adenocarcinoma; mDOR = median duration of response; mPFS = median progression-free survival. 1Elmova et al. ASCO GI 2023; 2Janjigian et. al., Lancet Oncol. 2023. Comparison used for current results of trastuzumab + chemo regimen from control arm of KN-811 trial (placebo + trastuzumab + chemo); 3Bang et. al., Lancet Oncol. 2010.
Zanidatamab + Chemo Demonstrated Promising Antitumor Activity in HER2+ 1L GEA Patients

Change in Target Lesion Size in Response-evaluable Patients with HER2-positive mGEA

Dotted lines indicate 20% increase and 30% decrease in sum of diameters of target tumors.

CA = primary tumor type; E = esophageal cancer; F = flat dosing regimen; FISH = fluorescence in situ hybridization; G = gastric cancer; IHC = immunohistochemistry; J = gastroesophageal junction adenocarcinoma; W = weight-based dosing regimen; ZDR = zanidatamab dosing regimen; zani = zanidatamab.

*1 patient is excluded from the figure because they did not have a postbaseline assessment of target lesions.

Change in Target Lesion Size Over Time in Response-evaluable Patients with HER2-positive mGEA

Dotted line indicates no change from baseline in sum of diameters of target tumor; zani = zanidatamab.

*1 patient is excluded from the figure because they did not have a postbaseline assessment of target lesions.

Source: Elimova et al, ASCO GI 2023. 1L = first line; mGEA = metastatic gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2.
Zanidatamab + Chemo Demonstrated Promising Early Overall Survival in HER2+ 1L GEA Patients

Progression-free Survival in Patients with HER2-positive mGEA

- Median PFS (95% CI), months: 12.5 (7.1, NE)

Overall Survival in Patients with HER2-positive mGEA

- Median OS (95% CI), months: NE (23.6, NE)
- 12-month OS (95% CI): 88% (73%, 95%)
- 18-month OS (95% CI): 84% (68%, 93%)

Source: Elimova et al, ASCO GI 2023. CI = confidence interval; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; NE = not evaluable; OS = overall survival; PFS = progression-free survival.
GEA Treatment Paradigm Highlights Unmet Need

Source: NCCN Guidelines. 1L = first line; ASCO GI = American Society of Clinical Oncology Gastrointestinal; EU5: Major EU markets, U.K, France, Germany, Spain, Italy; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; PD-L1 = programmed cell death protein 1; T-DXd = trastuzumab deruxtecan, or Enhertu®.

Keytruda awaiting full approval in EU5/Japan; Japan uses different chemo regimen from U.S.

Key ongoing Jazz trials

March 2024
Zanidatamab + Tislelizumab + Chemo in 1L GEA: Observed Clinical Activity and Benchmarks

1L = first line; cORR = confirmed objective response rate; GEA = gastroesophageal adenocarcinoma; mDOR = median duration of response; mPFS = median progression-free survival. 1\textsuperscript{1}Zanidatamab + tislelizumab + chemotherapy study done in collaboration with partner BeiGene. Lee et. al., ESMO 2023; \textsuperscript{2}Elimova et al, ASCO GI 2023; \textsuperscript{3}Janjigian et. al., Lancet Oncol. 2023; \textsuperscript{4}Bang et. al., Lancet Oncol. 2010.
Zanidatamab + Chemo + Tislelizumab Improves Durability

**Treatment Duration and Response**

**Duration of Response**

- Events: 12 (40.0%)
- Median: 22.8 months (95% CI: 7.4, NE)

**Progression-Free Survival**

- Events: 17 (51.5%)
- Median: 16.7 months (95% CI: 8.2, NE)

Note: Zanidatamab + tislelizumab + chemotherapy study done in collaboration with partner BeiGene. Lee et al., ESMO 2023.
HERIZON-GEA-01: Randomized Phase 3 Study of Zanidatamab + Chemotherapy ± I/O vs Trastuzumab + Chemotherapy in 1L Metastatic GEA

**Primary Endpoint:**
- PFS
- OS

**Secondary / Exploratory Endpoints:**
- ORR
- DOR
- Safety
- HRQoL

**Study Design**
- Unresectable locally advanced or metastatic gastroesophageal adenocarcinoma (stomach, GEJ, esophagus)
- HER2 status:
  - IHC3+ or ICH2+/ISH+\(^1\)
  - Any PD-L1 status
- No prior therapy for advanced disease
- Open-label with disease assessments per Blinded Independent Central Review (BICR)
- 1:1:1 randomization (total N = 918)
- Investigator choice of chemotherapy
- Stratification by region, HER2 status, and ECOG performance status

**Arm A**
- trastuzumab + SOC chemotherapy\(^2\)
- N=306

**Arm B**
- zanidatamab + SOC chemotherapy\(^2\)
- N=306

**Arm C**
- zanidatamab + tislelizumab + SOC chemotherapy\(^2\)
- N=306

ECOG PS = Eastern cooperative oncology group performance status scale; DOR = duration of response; GEJ = gastroesophageal juncture; HER2 = human epidermal growth factor receptor 2; HRQoL = health-related quality of life; mOS: median overall survival; mPFS: median progression free survival; RECIST: response evaluation criteria in solid tumors \(^1\)Per central testing based on results from new or archival tumor tissue, using VENTANA assays (4B5 and Dual ISH); \(^2\)SOC trastuzumab and chemotherapy (CAPOX or FP) are per typical dosing.
Rob Iannone, M.D., M.S.C.E.

Executive Vice President, Global Head of Research & Development
GEA Treatment Paradigm Highlights Unmet Need

**Current resectable treatment pathway does not differ on HER2 status**

### Gastric and esophageal adenocarcinoma

#### Resectable
- Neoadjuvant therapy
  - Chemo
  - Chemo + Radiation
- Surgery
  - Zanidatamab Potential

#### Adjuvant therapy
- Chemo
- Chemo + Radiation
- Nivolumab
  - Zanidatamab Potential

#### HER2+ Unresectable, locally advanced / metastatic GEA

- HER2+ 1L Unresectable
  - PD-L1+
  - Trastuzumab + pembrolizumab + chemo (KEYNOTE-811)
  - Zanidatamab ± tislelizumab + chemo (HERIZON-GEA-01)

- HER2- Unresectable
  - PD-L1-
  - Trastuzumab + chemo
  - Zanidatamab + chemo (HERIZON-GEA-01)

#### HER2+ 2L Unresectable
- T-DXd

**Key ongoing Jazz trials**

**Zanidatamab Opportunity**

Source: NCCN Guidelines. 1L = first line; ASCO GI = American Society of Clinical Oncology Gastrointestinal; EU5: Major EU markets, U.K, France, Germany, Spain, Italy; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; PD-L1 = programmed cell death protein 1; T-DXd = trastuzumab deruxtecan, or Enhertu®.

Keytruda awaiting full approval in EU5/Japan; Japan uses different chemo regimen from U.S.
GEA Represents a Significant Unmet Need

GEA opportunity of
~63,000 cases annually\(^1\)
in U.S., Europe\(^2\) and Japan

\(\sim 8,000\) HER2+ GEA patients annually\(^1\)

GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; HER2+ = IHC3+ or IHC2+/ISH+; IHC = immunohistochemistry. \(^1\)Incidence sources: Kantar reports, ToGA surveillance report; SEER, cancer.gov; ClearView Analysis; GLOBOCAN; Data on file; \(^2\)Major markets: U.K, France, Germany, Spain, Italy. Note: HER2+ BTC patients in Jazz controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd.
Zanidatamab Development Timeline in GEA

2024

- Targeting top-line PFS data from HERIZON-GEA-01

2025+

- Potential adoption in compendia and guideline recommendations
- Submit sBLA in 1L GEA
- Potential development in neoadjuvant / adjuvant GEA population

1L = first line; GEA = gastroesophageal adenocarcinoma; PFS = progression-free survival; sBLA = supplemental biologics license application.
Zanidatamab in Breast Cancer

Significant Potential in Early- to Late-Line Breast Cancer
Zanidatamab Opportunity in Early- and Late-Stage Breast Cancer

Expect to initiate Phase 3 breast cancer trial in patients who have progressed on T-DXd in 2H24

### Advanced Breast Cancer

<table>
<thead>
<tr>
<th>Zanidatamab + Physician’s Choice Chemotherapy</th>
<th>Zanidatamab + CDK4/6i + fulvestrant</th>
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<tbody>
<tr>
<td>Preclinical data: <strong>Additive antitumor effects</strong> when zanidatamab combined with wide range of chemo agents.</td>
<td><strong>CyclinD1-CDK4 pathway</strong> interacts with HER2 and ER pathways, <strong>mediating resistance</strong> to HER2 therapy.</td>
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**ZW25-101 trial: zanidatamab + chemo**
- **HER2+ metastatic BC**
- Median of 2 prior regimens (n = 24)
- Included patients refractory to trastuzumab + pertuzumab, T-DXd, other
  - **cORR:** 36.4%
  - **mPFS:** 7.3 months
- Activity of other anti-HER2 agents not defined after progression on T-DXd

**ZW25-202 Trial: zanidatamab + CDK4/6i + fulvestrant**
- Late-stage metastatic population
- **cORR:** 35%
- **mDOR:** 15 months
- **mPFS:** 12 months
- **Chemo-free regimen:** manageable toxicity profile address HER2 and ER biology

### Early Breast Cancer

**Neoadjuvant Therapy**

Opportunity to **improve pCR rate and reduce toxicity** of post-surgery therapy in the curative setting.

Zanidatamab: **Favorable safety profile** as monotherapy and in combination.

**POC trial: node neg, early-stage HER2+ BC**
- **Zanidatamab neoadjuvant therapy** prior to surgery
- **Significant efficacy:** 30% **pCR rate**

---

**BC** = breast cancer; **cORR** = confirmed objective response rate; **ER** = estrogen receptor; **HER2** = human epidermal growth factor receptor 2; **mDOR** = median duration of response; **mPFS** = median progression-free survival; **pCR** = pathological complete response; **POC** = proof of concept; **T-DXd** = trastuzumab deruxatecan, or Enhertu®.

Zanidatamab in Advanced mBC

Potential to Address Unmet Need After Progression on T-DXd
Current HER2+ Advanced Breast Cancer Treatment Paradigm

Cleopatra regimen and T-DXd currently favored in current HER2+ advanced treatment paradigm

1L
- Trastuzumab + pertuzumab + taxane (THP / “Cleopatra”)

2L
- T-DXd (anti-HER2 ADC)
- Tucatinib + trastuzumab + capecitabine

3L
- T-DM1 (anti-HER2 ADC)
- Other anti-HER2 Tx ± chemo
- Tucatinib + capecitabine + trastuzumab
- Anti-HER2 mAb + TKI

4L+
- Margetuximab + chemo
- Neratinib + chemo
- Trastuzumab + chemo
- Chemo alone

Preferred for patients with active brain metastases

If not received in 2L

Sources: UpToDate, NCCN Guidelines 2023; 1/2/3/4L = First/second/third/fourth line; ADC = antibody drug conjugate; HER2 = human epidermal growth factor receptor 2; T-DM1 = trastuzumab emtansine, Kadcyla®; T-DXd = trastuzumab deruxtecan, or Enhertu®; TKI: tyrosine kinase inhibitor.
Activity of Other Anti-HER2 Agents not Defined After Progression on T-DXd

- If T-DXd becomes 1L SoC as expected, 2L treatment will be undefined as currently having no approved HER2-targeted options to have demonstrated efficacy in this setting
- There will be a need for an effective post T-DXd therapy in 2L advanced BC

Sources: UpToDate, NCCN Guidelines 2023; 1/2/3/4L = First/second/third/fourth line; ADC = antibody drug conjugate; HER2 = human epidermal growth factor receptor 2; T-DM1 = trastuzumab emtansine, Kadcyla®; T-DXd = trastuzumab deruxtecan, or Enhertu®; THP = trastuzumab + pertuzumab + taxane; TKI: tyrosine kinase inhibitor.
Zanidatamab is Active in HER2+ mBC Patients Across Multiple Lines of Treatment Regardless of HR Status or Combination Therapy

<table>
<thead>
<tr>
<th>HER2 and HR status</th>
<th>1L mBC</th>
<th>3L+ mBC</th>
<th>3L+ mBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2+, HR+/-</td>
<td>BGB-A317-ZW25-101 (BC Cohorts 1a &amp; 1b)(^1)</td>
<td>ZW25-101 (Part 3)(^2)</td>
<td>ZW25-202(^3)</td>
</tr>
<tr>
<td>Regimen</td>
<td>zanidatamab + docetaxel</td>
<td>zanidatamab + select chemotherapies(^4)</td>
<td>zanidatamab + palbociclib + fulvestrant</td>
</tr>
<tr>
<td>N (HER2+)</td>
<td>37 (33 evaluable)</td>
<td>24 (22 evaluable)</td>
<td>51 (32 ccHER2+)</td>
</tr>
<tr>
<td>cORR n (%)</td>
<td>19 (90.9)</td>
<td>8 (36.4)</td>
<td>16 (35)</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(75.7, 98.1)</td>
<td>(13.9, 54.9)</td>
<td>(21, 50)</td>
</tr>
<tr>
<td>DOR, months</td>
<td>Median</td>
<td>NE</td>
<td>NA</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(12.1, NE)</td>
<td>(1.6, 22.1+)</td>
<td>(12, 25)</td>
</tr>
<tr>
<td>PFS, months</td>
<td>Median</td>
<td>NA</td>
<td>7.3</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>NA</td>
<td>(3.6, NE)</td>
<td>NA</td>
</tr>
</tbody>
</table>

cORR = confirmed objective response rate; CI = confidence interval; DOR = duration of response; HER2 = human epidermal growth factor receptor 2; mBC = metastatic breast cancer; NA = not applicable. NE = not estimable; PFS = progression-free survival.\(^1\) Data from BGB-A317-ZW25-101 study presented by BeiGene. Wang et. al. ASCO 2023; \(^2\)Bedard et. al., SABCS 2021; \(^3\)Escrivá-de-Romani S et al, SABCS 2023; \(^4\)Paclitaxel, capecitabin, vinorelbine.
Zanidatamab Plus Chemo is Active in Heavily Pre-treated HER2+ mBC Patients Compared to Other Regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>ZW25-101¹</th>
<th>Sophia Study²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zanidatamab + chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR</td>
<td>36.4% (CI 13.9 – 54.9)</td>
<td>14%</td>
</tr>
<tr>
<td>mDOR</td>
<td>NE (1.6 - 22.1+)</td>
<td>7.0 months</td>
</tr>
<tr>
<td>mPFS</td>
<td>7.3 months (95% CI: 3.6-NE)</td>
<td>4.4 months (95% CI: 4.1-5.5)</td>
</tr>
</tbody>
</table>

Phase 2 Data Demonstrates Activity in Patients Previously Treated with HER2-Targeted Therapies, Including T-DXd

Zanidatamab + Fulvestrant + CDK4/6i Efficacy of Treatment by Best Overall Response

Prior treatment with T-DXd

-30% and +20% change in tumor size.

Source: Escrivá-de-Romani S et al, SABCS 2023. T-DXd = trastuzumab deruxtecan, or Enhertu®.

Note: Best overall response includes patients with measurable disease. *All patients received prior trastuzumab and taxane.* Indicates patients with unconfirmed partial responses. Dotted lines indicate -30% and +20% change in tumor size. Source: Escrivá-de-Romani S et al, SABCS 2023. T-DXd = trastuzumab deruxtecan, or Enhertu®.
## Treatment After Progression on T-DXd is an Uncharted Space of Unmet Need

<table>
<thead>
<tr>
<th>Opportunity</th>
<th>Zanidatamab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
<td><strong>Opportunity:</strong> Patients want a better treatment option that is effective and maintains quality of life. <strong>Zanidatamab:</strong> MOA, clinical efficacy, and safety profile are advantageous for use after progression on T-DXd</td>
</tr>
<tr>
<td><strong>2</strong></td>
<td><strong>Opportunity:</strong> Physicians are looking for an answer to the sequencing dilemma and therapies indicated after progression on T-DXd. <strong>Zanidatamab:</strong> Goal of generating robust zanidatamab data to fill gaps in sequencing gap after progression T-DXd</td>
</tr>
<tr>
<td><strong>3</strong></td>
<td><strong>Opportunity:</strong> Zanidatamab has potential to be the 1st HER2-targeted therapy to demonstrate efficacy and safety after progression on T-DXd. <strong>Zanidatamab:</strong> Plan to launch Phase 3 study in patients who have progressed on T-DXd</td>
</tr>
</tbody>
</table>

HER2 = human epidermal growth factor receptor 2; MOA = mechanism of action; T-DXd = trastuzumab deruxtecan, or Enhertu®.
Randomized Phase 3 Study of Zanidatamab + Chemotherapy in Post T-DXd Patients with HER2+ Advanced BC

Inclusion Criteria:

- Patients with HER2+ BC whose disease has progressed on previous T-DXd treatment
- No more than 4 prior lines of HER2-directed therapies in metastatic setting
- Based on the patient eligibility, institutional and local guidelines, and physician's choice, all approved treatments are allowed as post T-DXd therapy, including pertuzumab, tucatinib-containing regimen, and T-DM1 prior to enrollment in the trial
- Patients with history of treated-CNS metastasis who are clinically stable are eligible
- At least 1 measurable lesion per RECIST version 1.1
- ECOG PS 0 or 1

Primary Endpoint:
- PFS

Secondary / Exploratory Endpoints:
- OS
- ORR
- Safety

N=550

ECOG PS = eastern cooperative oncology group performance status; mBC = metastatic breast cancer; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; RECIST = Response Evaluation Criteria In Solid Tumors; T-DM1 = trastuzumab emtansine, Kadcyla®; T-DXd = trastuzumab deruxtecan, or Enhertu®.
Potential HER2+ Advanced BC Treatment Paradigm: Post T-DXd Uncharted Space of Unmet Need

Sources: UpToDate, NCCN Guidelines 2023.1/2/3/4L = First/second/third/fourth line; ADC = antibody drug conjugate; HER2 = human epidermal growth factor receptor 2; T-DM1 = trastuzumab emtansine, Kadcyla®; T-DXd = trastuzumab deruxtecan, or Enhertu®; TKI: tyrosine kinase inhibitor.
Zanidatamab in HER2+/HR+ Advanced BC

Potential Chemo-Free Option for HER2+/HR+ Patients
Santiago Escrivá-de-Romaní, M.D.

Medical Oncologist, Breast Cancer Unit
Vall d’Hebron Institute of Oncology
**HER2+/HR+ Late-Stage Breast Cancer Treatment Paradigm**

1L

- trastuzumab + pertuzumab + taxane → trastuzumab + pertuzumab + ET
- **T-DXd** (anti-HER2 ADC)

2L

- T-DM1 (anti-HER2 ADC)
- Tucatinib + trastuzumab + capcitabine

3L

- Other anti-HER2 Tx ± chemo
- Tucatinib + capcitabine ± trastuzumab
- Anti-HER2 mAb + TKI
- **T-DXd** (anti-HER2 ADC)
- Margetuximab + chemo
- Neratinib + chemo
- Trastuzumab + chemo
- Chemo alone

4L+

- May be preferred for patients with active brain metastases

**Note:** standard approach is to treat HR+ patients with HER2+ treatment paradigm with possible addition of ET to anti-HER2 regimens

- Current treatment paradigm does not take full advantage of HR status and potential synergy between blocking HR and HER2 pathways
- Unmet need will remain following completion of PATINA* trial (1L maintenance) regardless of outcome

*PATINA trial evaluating efficacy and safety of the addition of Palbociclib to anti-HER2 treatment and ET maintenance after induction treatment in 1L HR+HER2+ mBC. Sources: UpToDate, NCCN Guidelines 2023. 1/2/3/4L = First/second/third/fourth line; ADC = antibody drug conjugate; HR = hormone receptor; HER2 = human epidermal growth factor receptor 2; ET: endocrine therapy (only used for hormone receptor positive breast cancer); T-DM1 = trastuzumab emtansine, Kadcyla®; T-DXd = trastuzumab deruxtecan, or Enhertu®; TKI: tyrosine kinase inhibitor.
HER2+/HR+ Advanced BC: Observed Clinical Activity and Benchmarks: Phase 2 Data from Zanidatamab + Fulvestrant + CDK4/6i

**cORR**

- **Zanidatamab + Palbociclib + Fulvestrant**: 48% ccHER2+; 35% Overall
- **MonarcHER (Abemaciclib + trastuzumab + fulvestrant)**: 33%
- **PATRICIA (Trastuzumab + palbociclib + letrozole)**: 21%

**mPFS**

- **Zanidatamab + Palbociclib + Fulvestrant**: 15m ccHER2+; 12m Overall
- **MonarcHER (Abemaciclib + trastuzumab + fulvestrant)**: 8.3m
- **PATRICIA (Trastuzumab + palbociclib + letrozole)**: 5.1m

**Notes:**
- BC = breast cancer; ccHER2+ = centrally confirmed HER2+; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; 1Escriva-de-Romani S et al. SABCS 2023; 2Tolaney SM et al. Lancet Oncol 2020; 3Ciruelos E et al. CCR 2020; * Note: Trial ongoing. Median (range) follow-up time: 16 (2-32) months.
Phase 2 Data from Zanidatamab + Fulvestrant + CDK4/6i Demonstrates Promising Antitumor Activity in Heavily Pretreated Patients Including Patients Receiving Prior T-DXd

Efficacy of Treatment by Best Overall Response

**cORR: 35%**
**ccHER2+ cORR: 48%**
**Non-ccHER2+: 10%**

Note: Best overall response includes patients with measurable disease. Source: Escrivá-de-Romani S et al, SABCS 2023. ccHER2+ = centrally confirmed HER2+; cORR = confirmed objective response rate; HER2 = human epidermal growth factor receptor 2; T-DXd = trastuzumab deruxtecan, or Enhertu®.

*Indicates patients with unconfirmed partial responses. Dotted lines indicate -30% and +20% change in tumor size.

All patients received prior trastuzumab and taxane.
Phase 2 Data from Zanidatamab + Fulvestrant + CDK4/6i Demonstrates Promising Durability and Progression-Free Survival

**Treatment Duration and Progression-Free Survival**

*Indicates patients with unconfirmed partial responses. Dotted line indicates 6 months. Source: Escrivá-de-Romani S et al, SABCS 2023. ccHER2 = centrally confirmed HER2; cCR = confirmed complete response; cPR = confirmed partial response; HER2 = human epidermal growth factor receptor 2; PD = progressive disease; PFS = progression-free survival; SD = stable disease; nCR/nPD = near complete response / near progressive disease.

**Median PFS: 12 months**
- ccHER2+: 15 months
- Non-ccHER2+: 8 months
Potential HER2+/HR+ Late-Stage Breast Cancer Treatment Paradigm

1L
- Zanidatamab Opportunity HER2+/HR+ 1L Maintenance (PATINA* Negative)

2L
- Zanidatamab Opportunity HER2+/HR+ (PATINA* Positive / T-DXd moves to 1L)
- Tucatinib + trastuzumab + capecitabine

3L
- T-DM1 (anti-HER2 ADC)
- Other anti-HER2 Tx ± chemo
- Tucatinib + capecitabine ± trastuzumab
- Anti-HER2 mAb + TKI
- T-DXd (anti-HER2 ADC)
- Margetuximab + chemo
- Neratinib + chemo
- Trastuzumab + chemo
- Chemo alone

4L+
- Zanidatamab Opportunity

Preferred for patients with active brain metastases

If not received in 1L/2L

*PATINA trial evaluating efficacy and safety of the addition of Palbociclib to anti-HER2 treatment and ET maintenance after induction treatment in 1L HR+/HER2+ mBC. Sources: UpToDate, NCCN Guidelines 2023. 1/2/3/4L = First/second/third/fourth line; ADC = antibody drug conjugate; HR = hormone receptor; HER2 = human epidermal growth factor receptor 2; ET: endocrine therapy (only used for hormone receptor positive breast cancer); T-DM1 = trastuzumab emtansine, Kadcyla®; T-DXd = trastuzumab deruxtecan, or Enhertu®; TKI: tyrosine kinase inhibitor.
Zanidatamab in Early-Stage Breast Cancer

Reducing Toxicity in a Curative Setting
Paula Pohlmann, M.D.
Department of Breast Medical Oncology,
Division of Cancer Medicine,
University of Texas MD Anderson Cancer Center
Opportunity to Improve Outcomes and Reduce Toxicity of Systemic Therapy in the Curative Setting

**HER2+ Early-Stage Treatment Paradigm**

**Size & Node Status**
- N0 and <2cm
- N+ or >2cm

**Surgery and Initial Neo/adj Tx**
- Surgical Resection +/- RT
- Neo adj chemo + tras + pert
- Surgical resection +/- RT

**Maintenance Adjuvant Tx**
- ET* + tras +/- pert
- ET* + tras +/- pert
- ET* + T-DM1

**Adj = adjuvant; HER2 = human epidermal growth factor receptor 2; ET = endocrine therapy; N+ = node positive; N0 = node negative; neo adj = neoadjuvant; pert = pertuzumab; RT = radiation therapy; T-DM1: trastuzumab emtansine, Kadcyla®; T-DXd = trastuzumab deruxatecan, or Enhertu®; tras = trastuzumab; Tx = treatment. *ET is only used for HR+; Sources: UpToDate, NCCN Guidelines 2023.**

**Potential long-term toxicity of cytotoxic agents:**
- Heart failure
- Secondary malignancies
- Disabling peripheral neuropathy
- Cognitive dysfunction
- Premature menopause
- Sexual dysfunction
- Infertility
- Liver dysfunction
Neoadjuvant Setting Is Key to Learning and to Personalizing Treatment

• Permits timely efficacy read-out
• Allows tailoring of treatment
  ✓ More for those who need it
  ✓ Less for those who do not
• Facilitates improvement and investigation of ‘success and failure’

Success Measurement
Residual Cancer Burden: Prognostic Value Beyond pCR

HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; pCR = pathologic complete response; RCB = residual cancer burden. Source: Symmans WF et al. RCB and long-term survival. JAMA Oncology 2021.
MDACC Trial Design Overview

- Single-arm open label study of zanidatamab in N0 neoadjuvant setting
- Study Details:
  - N = 20 → 40
  - HER2+ breast cancer
  - Any HR status
  - Early Stage
    - Tumor size > 1 cm ≤ 3cm
    - Node negative

Diagnosis of low-risk BC

Cohort 1
- zanidatamab monotherapy
  - 20 mg/kg every 2 weeks x 10 doses (5 cycles; each cycle = 4 weeks)

Cohort 2
- zanidatamab + chemotherapy

Surgical Resection

Adjuvant post surgical treatment as per treating physician’s choice

Note: MDACC trial being done in collaboration with MD Anderson Cancer Center (MDACC). N0 = node negative; BC = breast cancer; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; N0 = node negative.
Zanidatamab Demonstrated Significant Efficacy in Early-Stage Breast Cancer

- Neoadjuvant zanidatamab for 3 cycles (6-10 doses) showed **significant efficacy** in patients with stage I node negative HER2+ BC
  - 50% pCR/RCB-1
  - 30% pCR
- Zanidatamab was well-tolerated with acceptable safety profile
  - No Grade 3 or Grade 4 TRAEs
- Trial ongoing

### Pathologic Response and Residual Cancer Burden

<table>
<thead>
<tr>
<th># Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCR/RCB-0</td>
<td>6</td>
</tr>
<tr>
<td>RCB-1</td>
<td>4</td>
</tr>
<tr>
<td>RCB-2</td>
<td>9</td>
</tr>
<tr>
<td>RCB-3</td>
<td>1</td>
</tr>
</tbody>
</table>

Source: Valero V. et al. SABCS, 2023. pCR = pathologic complete response; RCB = residual cancer burden; pCR = pathologic complete response; RCB = residual cancer burden; TRAE = treatment-related adverse event.
Zanidatamab Selected for Inclusion in I-SPY 2 Studies

- Single agent zanidatamab in neoadjuvant setting (Block A)
- Planned enrollment N=100
- Will provide information on zanidatamab monotherapy in N0 and N+ patients
- I-SPY2 platform study utilizes an adaptive trial design and early surrogate efficacy endpoints (MRI functional tumor volume/FTV & pCR) allowing for efficient enrollment and faster initial efficacy results

Note: Pre-I SPY2 executed by Quantum Leap Health Collaborative under academic and regulatory leadership in collaboration with Pharma Companies.
PRE-I-SPY 2 Study Design Evaluating Zanidatamab + Tucatinib

- PRE-ISPY/Phase 1b multisite platform to evaluate single agents or combinations in a metastatic setting to move promising drugs into the I-SPY 2 SMART Neoadjuvant Design Trial and/or other trials in a timely manner
- Studying zanidatamab + tucatinib
- Designed to generate proof-of-concept data for expansion in the companion I-SPY2 Trial in the neo-adjuvant setting
- N = 12 in Part 1 dose finding and N=12 in Part 2 dose expansion
- Implications for indications outside breast cancer (eg, CRC)

Primary Endpoint:
- Dose finding / RP2D
- Safety / tolerability
- Preliminary efficacy

Secondary / Exploratory Endpoints:
- Preliminary PFS, DOR, CBR
- PK
- Translational Biomarkers

Note: Pre-I SPY2 executed by Quantum Leap Health Collaborative under academic and regulatory leadership in collaboration with Pharma Companies. CBR = clinical benefit rate; DOR= Duration of Response; N+ = node positive; N0 = node negative; PFS = progression-free survival; PK = pharmacokinetics; RP2D = recommended Phase 2 dose.
Goal of Reducing Toxicity in a Curative Setting

**HER2+ Early-Stage Treatment Paradigm**

- **Size & Node Status**
  - N0 and <2cm
  - N+ or >2cm

- **Surgery and Initial Neo/adj Tx**
  - Zanidatamab Opportunity
  - Surgical Resection +/- RT

- **Maintenance Adjuvant Tx**
  - ET* + tras +/- pert
  - ET* + T-DM1

- **No residual disease after neoadjuvant treatment**
  - ET* + tras +/- pert

- **Residual disease after neoadjuvant treatment**
  - ET* + T-DM1

---

**Adj = adjuvant; HER2 = human epidermal growth factor receptor 2; ET = endocrine therapy; N+ = node positive; N0 = node negative; neo adj = neoadjuvant; pert = pertuzumab; RT = radiation therapy; T-DM1: trastuzumab emtansine, Kadcyla®; T-DXd = trastuzumab deruxtecan, or Enhertu®; tras = trastuzumab; Tx = treatment. *ET is only used for HR+; Sources: UpToDate, NCCN Guidelines 2023.**
Zanidatamab Development in Breast Cancer
Building Patient Value in Early- and Late-Stage Breast Cancer

**Program**

**Neoadjuvant Node-Negative**
- Goal of **reducing toxicity** in adjuvant setting

**Neoadjuvant Node-Positive (I-SPY 2)**
- Patients and prescribers **want to reduce chemotherapy use** due to side effects, even for high-risk patients

**Late-Stage After Progression on T-DXd**
- No clinically validated **treatment option** for patients who progress or cannot tolerate T-DXd

**Late-Stage Combination with CDK4/6i + Fulvestrant**
- In HER2+/HR+ BC, treatment is based on HER2 status with limited consideration of estrogen therapies

**Unmet Need**

**Strategy**

**ESTABLISH** a new better-tolerated standard of care for low-risk patients in NeoAdj/Adj with zanidatamab monotherapy

**IMPROVE** pCR rates and reduce chemotherapy burden in adjuvant setting by replacing Herceptin and Perjeta and potential to de-escalate chemotherapy (chemo-free combinations)

**ADDRESS** high unmet need for patients who progress or cannot tolerate T-DXd in prior lines

**SHIFT** mindset from single HER2+ treatment focus in late-lines to Hormone Receptor (HR+) status plus HER2+ with a chemo free option

---

BC = breast cancer; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; NeoAdj/Adj = neoadjuvant / adjuvant setting; T-DXd = trastuzumab deruxtecan, or Enhertu®.
Zanidatamab Development Timeline in BC

2024

- Initiate Phase 3 trial in patients who have progressed after T-DXd
- Continued data generation in Phase 2 HR+/HER2+ (ZW25-202 study)
- Continued data generation in early-stage BC
  - I-SPY 2 Trial
  - MDACC Collaboration

2025+

- Potential registrational program in HR+/HER2+ patients, including contribution of components
- Continued data generation across lines of therapy

BC = breast cancer; HR+/HER2+ = hormone receptor positive / human epidermal growth factor receptor 2 positive; MDACC = MD Anderson Cancer Center; T-DXd = trastuzumab deruxtecan, or Enhertu®.
Zanidatamab Commercial Development

Path to $2B+ Peak Potential
Abizer Gaslightwala

Senior Vice President, Jazz Oncology
U.S. Business Unit Head
Zanidatamab: De-Risked Near-Term Opportunity with $2B+ Peak Potential

1st to market in BTC¹

- Familiarize physicians with zanidatamab treatment
- Initiated BLA submission in 4Q23
- Initiated confirmatory trial in 1L BTC
- Commercial launch preparations for 2025 or earlier

~12,000
BTC cases annually² in U.S., Europe³ and Japan

¹1L = first line; 2L = second line; BC = breast cancer; BLA = biologics license application; BTC = biliary tract cancer; FDA = Food and Drug Administration; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; HR+ = hormone receptor positive; NSCLC = non-small cell lung cancer; OS = overall survival; PD-L1 = programmed cell death ligand 1; T-DXd = trastuzumab deruxtecan. ²Pending regulatory approvals; ³Incidence sources: Kantar reports, ToGA surveillance report; SEER, cancer.gov; ClearView Analysis; GLOBOCAN, Data on file; ¹Major markets: U.K, France, Germany, Spain, Italy. ²Incidence source estimates derived from multiple sources: Decision Resources Group, Kantar Health, Jazz Market Research, data on file; ³Funda Meric-Bernstam et al, Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 1, dose-escalation and expansion study, The Lancet Oncology, Volume 23, Issue 12, 2022, Pages 1558-1570, ISSN 1470-2045, https://doi.org/10.1016/S1470-2045(22)00621-0. Note: HER2+ BTC patients in Jazz controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd.
Zanidatamab: De-Risked Near-Term Opportunity with $2B+ Peak Potential

1st to market in BTC¹

- Familiarize physicians with zanidatamab treatment
- Initiated BLA submission in 4Q23
- Initiated confirmatory trial in 1L BTC
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~12,000
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1L = first line; 2L = second line; BC = breast cancer; BLA = biologics license application; BTC = biliary tract cancer; FDA = Food and Drug Administration; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; HR+ = hormone receptor positive; NSCLC = non-small cell lung cancer; OS = overall survival; PD-L1 = programmed cell death ligand 1; T-DXd = trastuzumab deruxtecan.

1Pending regulatory approvals; ²Incidence sources: Kantar reports, ToGA surveillance report; SEER, cancer.gov; ClearView Analysis; GLOBOCAN, Data on file; ³Major markets: U.K, France, Germany, Spain, Italy. Incidence source estimates derived from multiple sources: Decision Resources Group, Kantar Health, Jazz Market Research, data on file. ⁴Funda Meric-Bernstam et al, Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 1, dose-escalation and expansion study, The Lancet Oncology, Volume 23, Issue 12, 2022, Pages 1558-1570, ISSN 1470-2045, https://doi.org/10.1016/S1470-2045(22)00621-0. Note: HER2+ BTC patients in Jazz controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd.

HER2-targeted agent of choice in GEA

- Address unmet need in PD-L1 negative population
- Replace trastuzumab in PD-L1 positive population
- Improved statistical power for OS analysis while maintaining PFS top-line readout target timing

~63,000
GEA cases annually² in U.S., Europe³ and Japan

~72,000
~63,000
Zanidatamab: De-Risked Near-Term Opportunity with $2B+ Peak Potential

1st to market in BTC¹
- Familiarize physicians with zanidatamab treatment
- Initiated BLA submission in 4Q23
- Initiated confirmatory trial in 1L BTC
- Commercial launch preparations for 2025 or earlier

~12,000
BTC cases annually² in U.S., Europe³ and Japan

~63,000
GEA cases annually² in U.S., Europe³ and Japan

Address unmet need post-T-DXd in BC
- Phase 3 Zanidatamab + chemo in post-T-DXd patients with HER2+ mBC
- Potential registrational program in HR+/HER2+ patients, including contribution of components
- Potential further development in neoadjuvant / adjuvant BC population

Her2-targeted agent of choice in GEA
- Address unmet need in PD-L1 negative population
- Replace trastuzumab in PD-L1 positive population
- Improved statistical power for OS analysis while maintaining PFS top-line readout target timing

~150,000
BC cases annually² in U.S., Europe³ and Japan

¹1L = first line; 2L = second line; BC = breast cancer; BLA = biologics license application; BTC = biliary tract cancer; FDA = Food and Drug Administration; GEA = gastroesophageal adenocarcinoma; HER2 = human epidermal growth factor receptor 2; HR+ = hormone receptor positive; NSCLC = non-small cell lung cancer; OS = overall survival; PD-L1 = programmed cell death ligand 1; T-DXd = trastuzumab deruxtecan
²Incidence sources: Kantar reports, ToGA surveillance report; SEER, cancer.gov; ClearView Analysis; GLOBOCAN, Data on file
³Major markets: U.K, France, Germany, Spain, Italy
⁴Incidence source estimates derived from multiple sources: Decision Resources Group, Kantar Health, Jazz Market Research, data on file
⁵Funda Meric-Bernstam et al, Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 1, dose-escalation and expansion study, The Lancet Oncology, Volume 23, Issue 12, 2022, Pages 1558-1570, ISSN 1470-2045, https://doi.org/10.1016/S1470-2045(22)00621-0. Note: HER2+ BTC patients in Jazz controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd.
Zanidatamab: De-Risked Near-Term Opportunity with $2B+ Peak Potential

1st to market in BTC¹
- Familiarize physicians with zanidatamab treatment
- Initiated BLA submission in 4Q23
- Initiated confirmatory trial in 1L BTC
- Commercial launch preparations for 2025 or earlier

~12,000 BTC cases annually² in U.S., Europe³ and Japan

HER2-targeted agent of choice in GEA
- Address unmet need in PD-L1 negative population
- Replace trastuzumab in PD-L1 positive population
- Improved statistical power for OS analysis while maintaining PFS top-line readout target timing

~63,000 GEA cases annually² in U.S., Europe³ and Japan

Address unmet need post-T-DXd in BC
- Phase 3 Zanidatamab + chemo in post-T-DXd patients with HER2+ mBC
- Potential registrational program in HR+/HER2+ patients, including contribution of components
- Potential further development in neoadjuvant / adjuvant BC population

~150,000 BC cases annually² in U.S., Europe³ and Japan

Broad potential in other HER2-targeted indications
- Broad potential beyond BTC, GEA, and BC in multiple HER2-expressing indications based on compelling clinical activity from early trials⁵
  - Colorectal
  - NSCLC
  - Ovarian
  - Endometrial
  - Pancreatic
  - Bladder
  - Salivary Gland
  - Ampullary
  - Other HER2-expressing solid tumors

Major markets: U.K, France, Germany, Spain, Italy. ¹Incidence source estimates derived from multiple sources: Decision Resources Group, Kantar Health, Jazz Market Research, data on file; ²Fundu Meric-Bernstam et al, Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 1, dose-escalation and expansion study, The Lancet Oncology, Volume 23, Issue 12, 2022, Pages 1558-1570, ISSN 1470-2045, https://doi.org/10.1016/S1470-2045(22)00621-0. Note: HER2+ BTC patients in Jazz controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd.
## Significant Commercial Opportunity with Multiple Expansion Indications

### 2024
- **BTC**
  - 2L fast-to-market strategy
  - Potential for accelerated approval in U.S. and EU
  - Initiated 1L confirmatory trial
- **GEA**
  - HERIZON-GEA-01 top-line data
- **BC**
  - Initiating Phase 3 in patients after progression on T-DXd in 2H24

### 2025
- **BTC**
  - Potential commercial launch 2025, or earlier
- **GEA**
  - HERIZON-GEA-01 full results
  - Potential development in neoadjuvant / adjuvant GEA population
- **BC**
  - HER2+/HR+ program

### 2026
- **GEA**
  - Potential 1L approval
  - Expanded market strategy
- **BC**
  - Continue BC development
  - Potential further development in neoadjuvant / adjuvant BC population

### 2027+
- **Potential Indications:**
  - Colorectal
  - NSCLC
  - Ovarian
  - Endometrial
  - Pancreatic
  - Bladder
  - Salivary Gland
  - Ampullary

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1L, 2L = first, second line therapy; BC = breast cancer; GEA = gastroesophageal adenocarcinoma; GI = gastrointestinal; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; NSCLC = non-small cell lung cancer; sBLA = supplemental biologics license application; T-DXd = trastuzumab deruxtecan, or Enhertu®.