

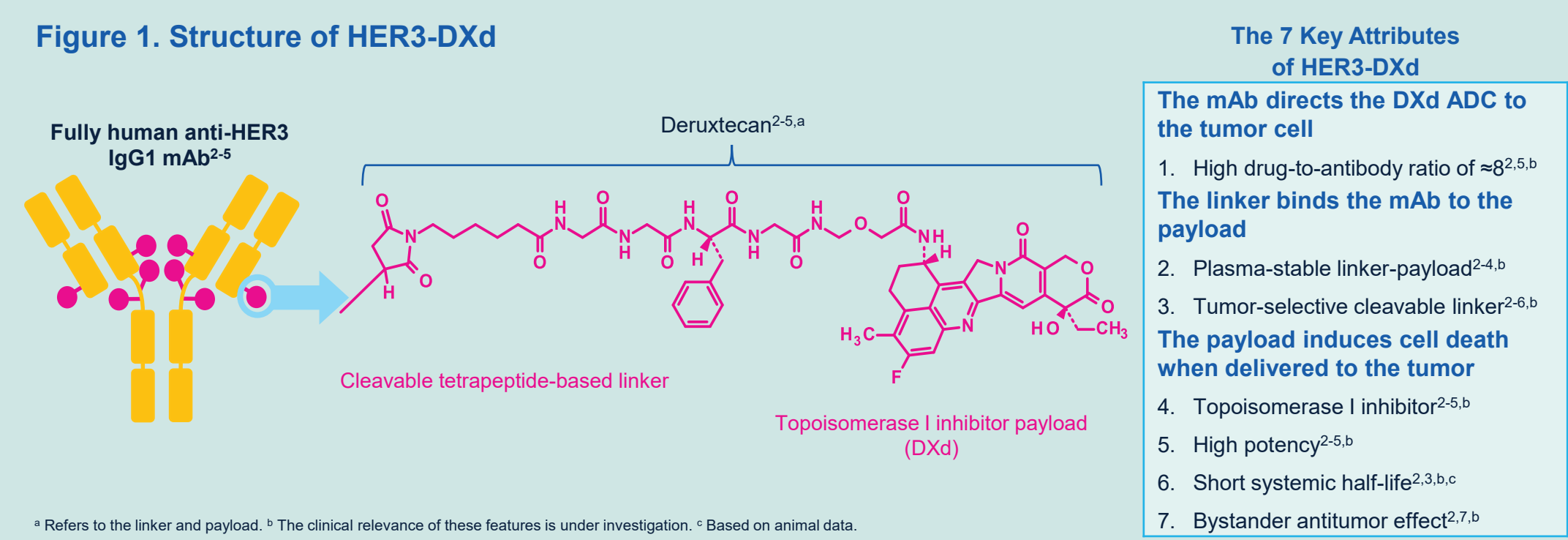
# HERTHENA-PanTumor01 (NCT06172478): Expansion of a Global Phase 2 Trial of HER3-DXd in Patients With Advanced/Metastatic HR+/HER2- Breast Cancer

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## BACKGROUND

- Increased tumor expression of human epidermal growth factor receptor 3 (HER3), a key member of the HER/EGFR family of receptor tyrosine kinases, is associated with poor clinical outcomes across multiple types of solid tumors, including HR+/HER2- breast cancer<sup>1</sup>
- Patritumab deruxtecan (HER3-DXd) is an antibody-drug conjugate composed of a human anti-HER3 monoclonal antibody linked to a topoisomerase I inhibitor payload via a stable tetrapeptide-based, tumor-selective, cleavable linker (Figure 1)<sup>2-4</sup>

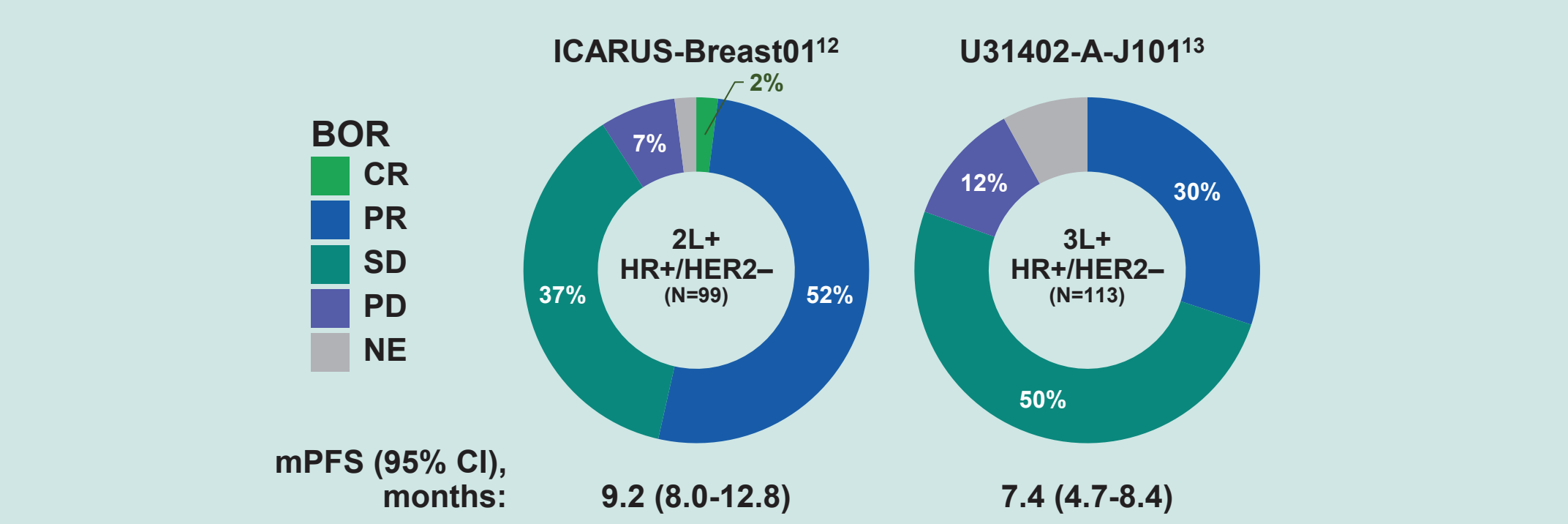


HER3-DXd has shown dose-dependent antitumor activity in various xenograft models of breast cancer, with activity seen across baseline HER3 levels, both in the presence and the absence of HER2 expression<sup>11</sup>

HER3-DXd has demonstrated clinically meaningful activity and a manageable safety profile in patients with advanced breast cancer across baseline tumor HER3 expression levels<sup>5,12-14</sup>

Antitumor activity was observed in HR+/HER2- metastatic breast cancer following progression on CDK4/6 inhibitors in the ICARUS-BREAST01 study, irrespective of baseline HER3 expression levels (ORR, 54%; 90% CI, 45%-62%),<sup>12</sup> as well as in the 3L setting for patients with HER3-expressing tumors, whose disease was refractory to current standard of care therapies from the U31402-A-J101 study (ORR, 30%; 95% CI, 22%-39%)<sup>13</sup>

Figure 2. Select Efficacy Data From Trials of HER3-DXd in Metastatic Breast Cancer<sup>12,13</sup>



HERTHENA-PanTumor01 (NCT06172478) is a global, multicohort, open-label, single-arm, phase 2 trial evaluating the efficacy and safety of HER3-DXd in patients with refractory, unresectable locally advanced or metastatic tumors<sup>15,16</sup>

This study includes 13 cohorts in total; 3 recently added cohorts (2L HER2- gastric cancer, non-AGA NSCLC, and metastatic breast cancer) are currently open for enrollment. Here we present details of the newly opened HR+/HER2- metastatic breast cancer cohort

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## STUDY DESIGN

### Key Eligibility Criteria for All Cohorts

- Previously treated, unresectable, stage III or IV metastatic disease
- Pretreatment biopsy
- No preselection based on HER3 expression

### HER+/HER2- breast cancer expansion cohort (n=90)

- The HERTHENA-PanTumor01 study includes 10 previously reported cohorts in multiple indications,<sup>15,16</sup> with 3 recently added expansion cohorts
- This poster presents the newly opened HR+/HER2- metastatic breast cohort
- Pathologically documented HER2-negative (IHC 0/1+ or IHC 2+/ISH negative) and HR-positive expression as classified by ASCO-CAP guidelines
- Prior treatment with only 1 line of chemotherapy for metastatic disease, with clinically or radiologically documented evidence of tumor progression on or after a CDK4/6 inhibitor combined with endocrine therapy<sup>a</sup>

- Tumor assessments will occur Q6W (±7 days) for the first 48 weeks, then Q12W (±14 days)
- Blood samples will be collected for biomarker, pharmacokinetic, and antidrug antibody analyses during treatment and at study discontinuation

<sup>a</sup>Prior treatment with phosphoinositide 3-kinase inhibitors, mechanistic target of rapamycin inhibitors, protein kinase B inhibitors also known as AKT-inhibitors and poly ADP ribose polymerase inhibitors are allowed.

## KEY ELIGIBILITY CRITERIA

### Inclusion Criteria

All cohorts

- Age ≥18 years
- Locally advanced unresectable or metastatic disease (not curable by surgery or radiation)
- ≥1 measurable lesion<sup>a</sup> (per RECIST version 1.1)
- Pretreatment tumor tissue sample of adequate quality<sup>b</sup>
- ECOG PS of 0 or 1
- Adequate bone marrow reserve and organ function

### HR+/HER2- breast cancer expansion cohort

- Locally advanced or metastatic HR+/HER2- disease (IHC 0/1+ or IHC 2+/ISH negative)<sup>c</sup>
- Disease progression during or after combined CDK4/6 inhibitor and endocrine therapy
- Only 1 prior line of chemotherapy for metastatic disease

### Exclusion Criteria

- Prior treatment with an anti-HER3 antibody or a topoisomerase I inhibitor (alone or as part of ADC therapy)
- Clinically severe respiratory compromise resulting from intercurrent pulmonary illnesses
- A history of ILD/pneumonitis requiring corticosteroid therapy or current or suspected ILD/pneumonitis
- Clinically active brain metastases or spinal cord compression,<sup>d</sup> or any history or current evidence of LMD

<sup>a</sup>On CT or MRI by investigator assessment. <sup>b</sup>From ≥1 lesion not previously irradiated and either performed since progression per RECIST 1.1 with the most recent systemic cancer therapy regimen, or freshly collected. Tumor tissue samples must contain ≥100 viable tumor cells. <sup>c</sup>As classified by ASCO-CAP guidelines. <sup>d</sup>Defined as being symptomatic or untreated or requiring therapy with corticosteroids or anticonvulsants.

## STUDY ENDPOINTS

### Primary Endpoint

- ORR as assessed by investigator per RECIST 1.1

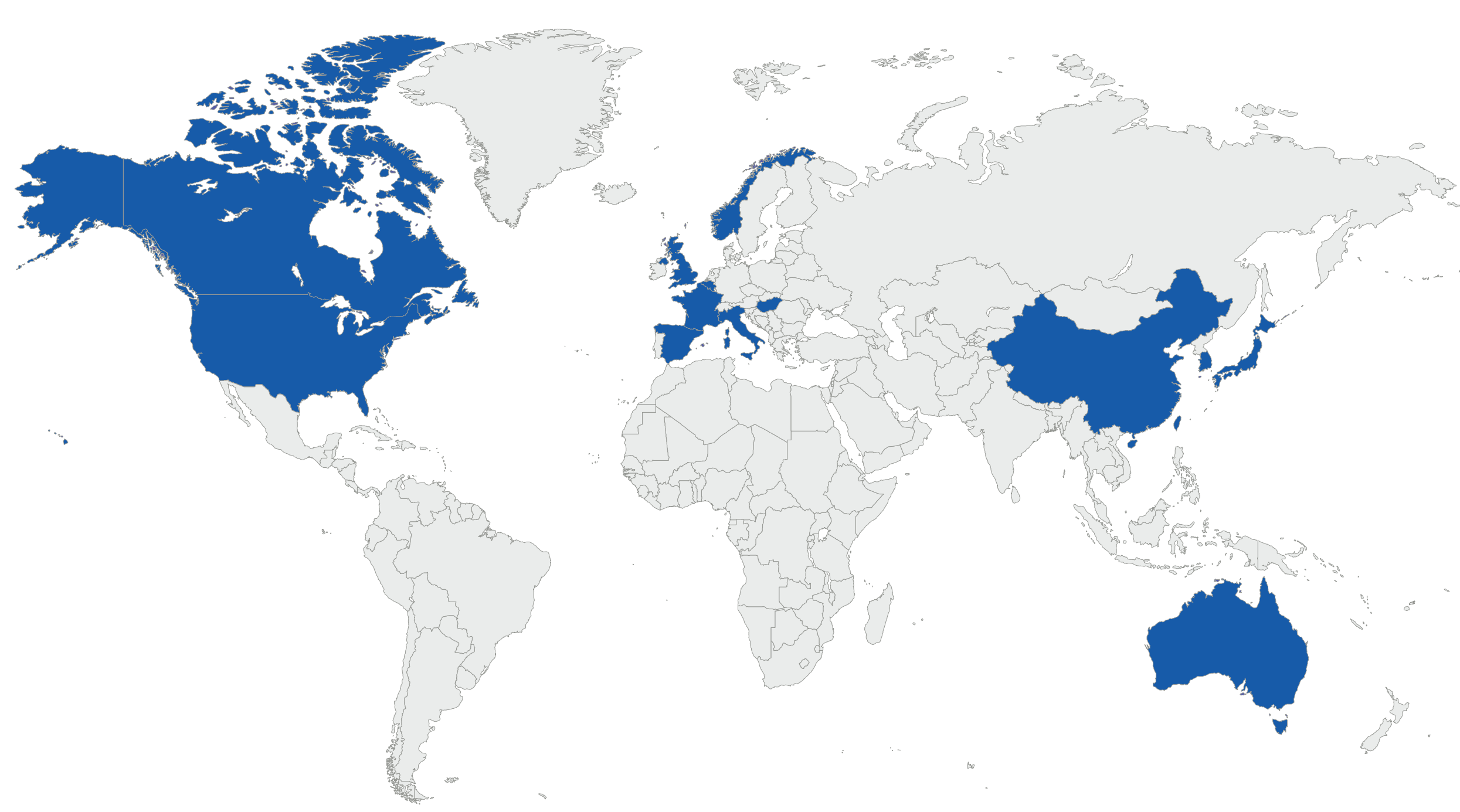
### Secondary Endpoints

- Safety and tolerability
- CBR,<sup>a</sup> DOR, DCR, TTR, and PFS as assessed by investigator per RECIST 1.1
- OS
- PK
- Correlation between HER3 protein expression by IHC and efficacy

<sup>a</sup>Defined as the proportion of patients with a best overall response of confirmed complete response, confirmed partial response, or stable disease lasting ≥183 days.

## ENROLLMENT STATUS

Recruitment for the breast cancer cohort is underway, with a planned enrollment of 90 patients in sites spanning North America, Europe, East Asia, and Australasia



## ABBREVIATIONS

2L, second line; 3L, third line; ADC, antibody-drug conjugate; AGA, actionable genomic alteration; ASCO-CAP, American Society of Clinical Oncology-College of American Pathologists; BOR, best overall response; CBR, clinical benefit rate; CDK4/6, cyclin-dependent kinase; CR, complete response; CT, computed tomography; DCR, disease control rate; DOR, duration of response; DXd, topoisomerase I inhibitor payload (an exatecan derivative); ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HER, human epidermal growth factor receptor; HR, hormone receptor; Ig, immunoglobulin; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; IV, intravenous; LMD, leptomeningeal disease; mAb, monoclonal antibody; mPFS, median PFS; MRI, magnetic resonance imaging; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetics; PR, partial response; Q3W, every 3 weeks; Q6W, every 6 weeks; Q12W, every 12 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TEAE, treatment-emergent adverse event; TTR, time to response.

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