

KANDELA-302: A Phase 3, Global, Open-Label, Randomized Study of the Selective CDK4 Inhibitor BGB-43395 + Letrozole vs CDK4/6 Inhibitors + Letrozole for First-Line Treatment of Advanced or Metastatic HR+/HER2– Breast Cancer

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Sara M. Tolaney,¹ Hope S. Rugo,² Zhimin Shao,³ Mario Campone,⁴ Yeon Hee Park,⁵ Naoki Niikura,⁶ Sherko Kuemmel,⁷ Heather L. McArthur,⁸ Alejandra Ragone,⁹ Hao Zheng,⁹ Hua-Xin Gao,⁹ Shom Goel¹⁰

¹Department of Medical Oncology, Dana Farber Cancer Institute, Boston, MA, USA; ²Department of Medical Oncology and Therapeutics Research, City of Hope, Duarte Cancer Center, Duarte, CA, USA; ³Department of Breast Surgery, Fudan University Shanghai Cancer Center, Shanghai, China; ⁴Department of Medical Oncology, Institut de Cancerologie de l'Ouest, Angers, France; ⁵Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; ⁶Department of Breast and Endocrine Surgery, Tokai University School of Medicine, Isehara, Japan; ⁷Breast Unit, Kliniken Essen-Mitte, Essen, Germany; ⁸Department of Medical Oncology, University of Texas Southwestern Medical Center, Dallas, TX, USA; ⁹BeOne Medicines, Ltd, San Carlos, CA, USA; ¹⁰Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

INTRODUCTION

- Hormone receptor (HR)+/human epidermal growth factor receptor 2 (HER2)– is the most common form of advanced/metastatic breast cancer (mBC), affecting 65%-75% of patients¹
- Cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) + endocrine therapy (ET) is a standard first-line (1L) therapy for patients with HR+/HER2– mBC
- Although the combination of CDK4/6i and ET has greatly improved the prognosis for patients with untreated HR+/HER2– mBC,^{2,3} an unmet need remains as the disease inevitably progresses
 - Furthermore, hematologic and other toxicities related to CDK4/6i therapy, which are potentially driven by CDK6 inhibition, limit the use of these therapies⁴
- The combination of a CDK4-selective inhibitor and aromatase inhibitors (AIs) may offer improved disease control and a decreased risk of adverse events in the 1L metastatic disease setting compared with current standard-of-care CDK4/6i in combination with AI^{4,5}
- BGB-43395, a potent, highly selective, orally available CDK4i, has shown robust antitumor activity with a favorable safety profile in preclinical models⁵ and a clinical evaluation⁶
 - Emerging clinical data from a Phase 1 study (NCT06120283) have demonstrated a favorable risk-benefit profile for BGB-43395 combined with letrozole when used as a 1L therapy for patients with HR+/HER2– mBC⁶
 - Notably, a low incidence and severity of hematologic toxicities was seen compared with CDK4/6i therapy, as well as promising antitumor activity at 400 mg twice daily⁶
 - Gastrointestinal (GI) toxicities were reduced by administering BGB-43395 with food, with meaningful reductions in all-grade treatment-related GI toxicities seen during the first two cycles, with lower rates of grade 1 GI toxicities and no grade ≥2 GI events⁶
- The KANDELA-302 (NCT07492641) trial aims to determine the efficacy and safety of BGB-43395 + letrozole (an AI) as 1L therapy for patients with HR+/HER2– mBC

STUDY DESIGN

- KANDELA-302 (NCT07492641) is an open-label, randomized, global, phase 3 study investigating the efficacy and safety of 1L BGB-43395 + letrozole vs investigator’s choice of CDK4/6i + letrozole for patients with HR+/HER2– mBC (**Figure 1**)

Inclusion criteria

- Histologically confirmed locally advanced/metastatic HR+/HER2– BC
- Aged ≥18 years
- ECOG PS ≤1
- Ability to provide an archived or fresh tumor biopsy

- Measurable disease per RECIST v1.1^a
- Adequate organ function
 - Premenopausal patients are required to receive a GnRH agonist, such as goserelin, while on therapy

Exclusion criteria

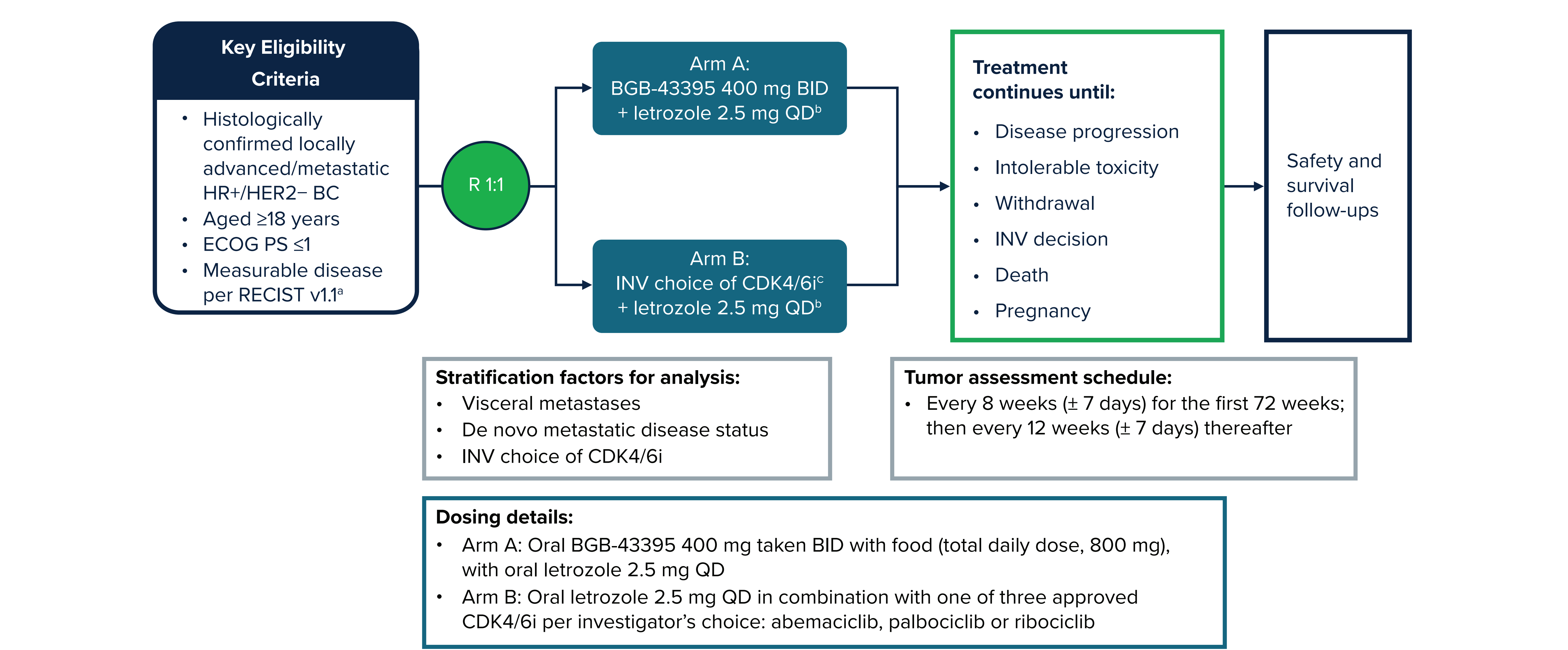
- Prior systemic anticancer treatment in the advanced or metastatic setting
- Prior ET ± CDK4/6i in the (neo)adjuvant setting with early recurrence (≤12 months)
- Prior CDK4- or CDK2-targeting therapies or investigational agents in any setting, except for oral SERDs

- Current visceral crisis
- Prior malignancies ≤3 years before enrollment
- Active infection
- History of ILD/pneumonitis
- Active LMD or uncontrolled brain metastases^b

^aIncluding evaluable bone-only disease. ^bStable central nervous system metastases are allowed if they show no evidence of progression, have been stable for ≥4 weeks, have no ongoing requirement for corticosteroid treatment, and have not received stereotactic or whole-brain radiation ≤14 days prior to study randomization.

Abbreviations: BC, breast cancer; CDK, cyclin-dependent kinase; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; GnRH, gonadotropin-releasing hormone; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; ILD, interstitial lung disease; LMD, leptomeningeal disease; RECIST, Response Evaluation Criteria in Solid Tumors; SERD, selective estrogen receptor degrader.

Figure 1. Study Design



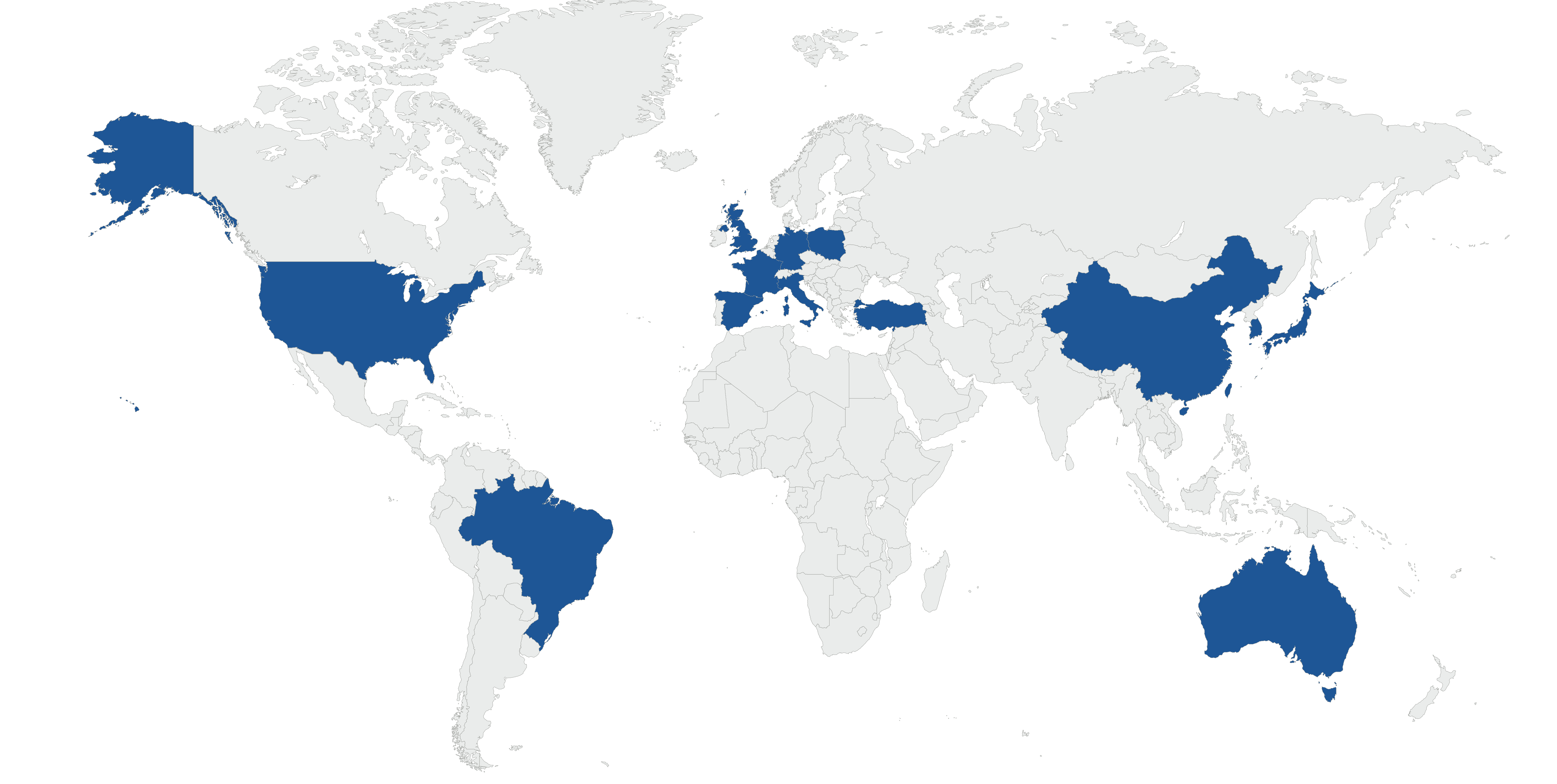
^aIncluding evaluable bone-only disease. ^bPremenopausal patients are required to receive a gonadotropin-releasing hormone agonist, such as goserelin, while on therapy. ^cApproved drugs only.

Abbreviations: BC, breast cancer; BID, twice daily; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; INV, investigator; QD, once daily; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.

ENROLLMENT STATUS

- As of August 2026, recruitment is underway across multiple sites in North America, South America, Europe, Asia, and Australia (**Figure 2**), with primary study completion expected in 2029 and final study completion by 2037; approximately 1056 patients will be enrolled

Figure 2. Map of Recruitment Areas



STUDY ENDPOINTS

Primary endpoint
• PFS as assessed by BICR^a
Secondary endpoint
• OS (key) • ORR as assessed by BICR^a • DOR as assessed by BICR^a • PFS as assessed by INV^a • CBR^{a,b} • TTR^a • PFS2 as assessed by INV • Safety • PROs^c
Exploratory endpoints
• PK and PD • PROs^d • Healthcare resource utilization • Biomarkers including, but not limited to, TK1 and ctDNA

^aPer RECIST v1.1. ^bDefined as the proportion of patients with a best overall response of confirmed complete response, confirmed partial response, or stable disease for ≥24 weeks. ^cChanges from baseline in global health status/quality of life, physical functioning, role functioning, nausea/vomiting scales, and diarrhea, as well as breast symptoms, arm symptoms, and systematic therapy side effect scales as measured by the European Organisation for Research and Treatment of Cancer-IL454. ^dChanges from baseline in the EuroQol EQ-5D-5L, Patient Global Impression of Symptom Severity BC, and patient-reported side effect burden as measured by patient-reported TSEB.

Abbreviations: BC, breast cancer; BICR, blinded independent central review; CBR, clinical benefit rate; ctDNA, circulating tumor DNA; DOR, duration of response; HEOR, health economics and outcomes research; INV, investigator; ORR, objective response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PK, pharmacokinetics; PRO, patient reported outcome; RECIST, Response Evaluation Criteria in Solid Tumors; TK1, thymidine kinase 1; TSEB, treatment-related side-effect burden; TTR, time to response.

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DISCLOSURES

SMT: Funding: Exelixis, OncoPep; Coordinating PI: AstraZeneca, Gilead; Local PI: Merck, Novartis, Genentech/Roche, Stemline/Menarini, Jazz Pharmaceuticals, NanoString, BMS, Daiichi Sankyo; Steering committee: Olema Pharmaceuticals; Consulting: Aadi BioPharma, Blueprint Medicines, Hengrui, Avenzo Therapeutics, Aktis Oncology, Celcuty, Samsung Bioepis, Tempus, Boundless Bio, Denali Therapeutics; Advisory board: Artios, AstraZeneca, Bayer, BMS, Daiichi Sankyo, Eisai, Eli Lilly, Genentech/Roche, Gilead, Menarini/Stemline, Merck, Sumitovant Biopharmaceuticals, Novartis, Pfizer, Reveal Genomics, Seagen, Jazz Pharma, Natera, Tango Therapeutics, Systimmune, eFFECTOR, Cullinan Oncology, Arvinas, Bicycle Therapeutics, Summit Therapeutics, BeOne Medicines, Ltd, BioNtech, Zuellig Pharma, Circle Pharma, Johnson & Johnson/Ambix, Launch Therapeutics, Mersana Therapeutics, Boehringer Ingelheim, Ottimo Pharma, Eli Lilly, Pfizer, Seagen; Travel support: Eli Lilly, Gilead Sciences, Jazz Pharmaceuticals, Arvinas, Genentech/Roche, AstraZeneca.

ACKNOWLEDGMENTS

The authors thank the patients and their families, investigators, co-investigators, and the study teams at each of the participating centers. This study was sponsored by BeOne Medicines, Ltd. Medical writing support was provided by Simon Foale, PhD, CMPP, of Nucleus Global, an Inizio company, and was supported by BeOne Medicines.