



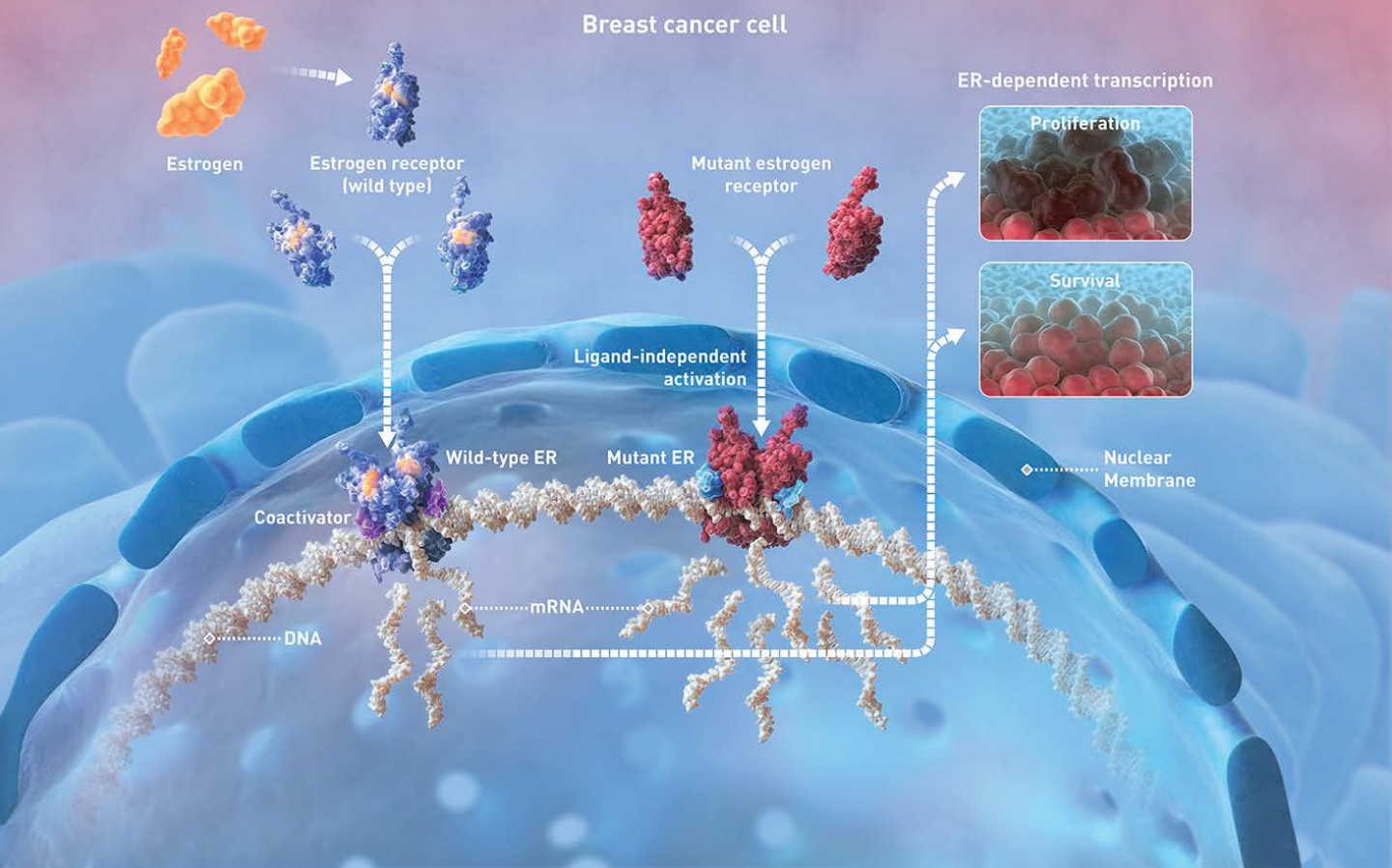
# IMLUNESTRANT (LY3484356)

## SELECTIVE ER DEGRADER

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# IMLUNESTRANT SELECTIVE ER DEGRADER (LY3484356) | MECHANISM OF ACTION<sup>1-4</sup>



Gladden AB, Diehl JA<sup>1</sup>; Patel HK, Bihani T<sup>2</sup>; Tecalco-Cruz AC, et al<sup>3</sup>; Wardell SE, et al<sup>4</sup>

**References:** 1. Gladden AB, Diehl JA. *J Cell Biochem.* 2005;96(5):906-913. 2. Patel HK, Bihani T. *Pharmacol Ther.* 2018;186:1-24. 3. Tecalco-Cruz AC, et al. *Cell Signal.* 2017;34:121-132. 4. Wardell SE, et al. *Clin Cancer Res.* 2015;21(22):5121-5130.

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## TARGET

Estrogen signaling plays an important role in organ development and growth. In certain cancers, abnormal estrogen signaling via the estrogen receptor is a component of tumor growth.<sup>1</sup> Disruption of estrogen signaling by selective estrogen receptor degraders (SERDs) is one of the treatment options for patients with estrogen-receptor-positive (ER+) cancers.

## MOLECULE

Imlunestrant is an orally available SERD that suppresses estrogen signaling and subsequently inhibits cell proliferation in ER-expressing tumor models.<sup>2,3</sup>

## CLINICAL DEVELOPMENT

Imlunestrant is being investigated in clinical trials in patients with ER+ breast cancer or endometrial cancer.

**References:** 1. Lee HR, et al. *Int J Mol Med.* 2012;29:883-890. 2. Bhagwat SV, et al. *Cancer Res.* 2021;81(13\_Suppl):1236. 3. VandeKopple M, et al. ESMO Breast Cancer Annual Congress; May 11-13, 2023; Berlin, Germany. Abstract 41P.

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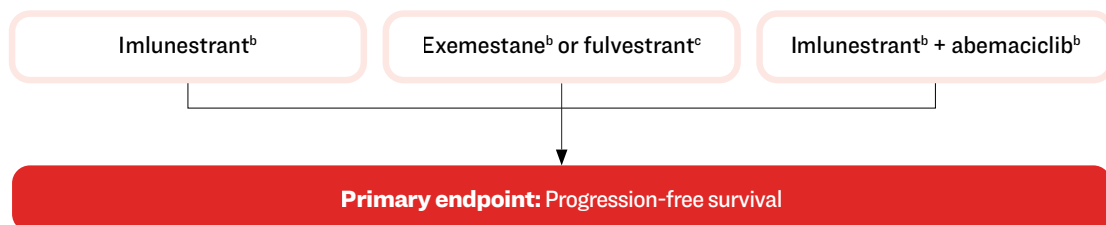
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# IMLUNESTRANT SELECTIVE ER DEGRADER (LY3484356)

## EMBER-3

**A Phase 3 Randomized, Open-Label Study of Imlunestrant, Investigator's Choice of Endocrine Therapy, and Imlunestrant Plus Abemaciclib in Patients With Estrogen-Receptor-Positive, HER2-Negative Locally Advanced or Metastatic Breast Cancer Previously Treated With Endocrine Therapy<sup>a</sup>**



<sup>a</sup>This clinical trial is being conducted globally. <sup>b</sup>Administered orally. <sup>c</sup>Administered intramuscularly.

**Abbreviation:** HER2=Human Epidermal Growth Factor Receptor 2.

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT04975308].

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## EMBER-3

**A Phase 3 Randomized, Open-Label Study of Imlunestrant, Investigator's Choice of Endocrine Therapy, and Imlunestrant Plus Abemaciclib in Patients With Estrogen-Receptor-Positive, HER2-Negative Locally Advanced or Metastatic Breast Cancer Previously Treated With Endocrine Therapy (Cont.)**

## KEY INCLUSION CRITERIA

- Diagnosis of estrogen-receptor-positive (ER+), HER2-negative locally advanced or metastatic breast cancer
- Disease that has demonstrated progression on or after an aromatase inhibitor alone or in combination with a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor
  - Patients are expected to have received prior treatment with a CDK4/6 inhibitor if this treatment is approved and can be reimbursed
- Must be deemed appropriate for treatment with endocrine therapy
- Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) evaluable disease (measurable disease and/or nonmeasurable bone-only disease)
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate renal, hematologic, and hepatic organ function
- If female, have a postmenopausal status by natural or surgical means or by ovarian function suppression
- Able to swallow capsules/tablets

## KEY EXCLUSION CRITERIA

- Prior treatment with chemotherapy (except for neoadjuvant/adjuvant chemotherapy), fulvestrant, or any investigational ER-directed therapy (including SERDs and non-SERDs), any PI3K, mTOR, or AKT inhibitor
- Visceral crisis, lymphangitic spread within the lung, or any evidence of leptomeningeal disease
- Symptomatic or untreated brain metastasis
- Serious preexisting medical conditions
- Known allergic reaction against any of the components of the study treatment

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT04975308].

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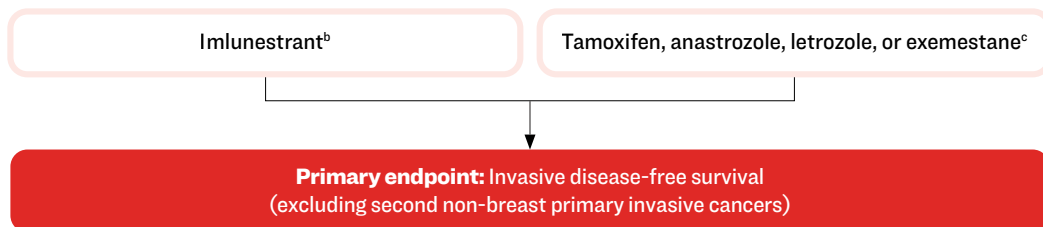
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# IMLUNESTRANT SELECTIVE ER DEGRADER (LY3484356)

## EMBER-4

**A Randomized, Open-Label, Phase 3 Study of Adjuvant Imlunestrant vs Standard Adjuvant Endocrine Therapy in Patients Who Have Previously Received 2 to 5 Years of Adjuvant Endocrine Therapy for ER+, HER2-Early Breast Cancer With an Increased Risk of Recurrence<sup>a</sup>**



<sup>a</sup>This clinical trial is being conducted globally. <sup>b</sup>Administered orally. <sup>c</sup>Endocrine therapy (investigator's choice of tamoxifen, anastrozole, letrozole, or exemestane) is administered per local approved label.

**Abbreviations:** ER=Estrogen Receptor; HER2=Human Epidermal Growth Factor Receptor 2.

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT05514054].

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## EMBER-4

**A Randomized, Open-Label, Phase 3 Study of Adjuvant Imlunestrant vs Standard Adjuvant Endocrine Therapy in Patients Who Have Previously Received 2 to 5 Years of Adjuvant Endocrine Therapy for ER+, HER2-Early Breast Cancer With an Increased Risk of Recurrence (Cont.)**

### KEY INCLUSION CRITERIA

- Diagnosis of estrogen-receptor-positive (ER+), HER2-negative (HER2-) early-stage, resected, invasive breast cancer without evidence of distant metastasis
- Participants must have received at least 24 months, but not more than 60 months, of any adjuvant endocrine therapy (ET) from time of adjuvant ET initiation
- Participants may have received neoadjuvant chemotherapy and/or targeted therapy with a cyclin-dependent kinase 4 and 6 (CDK4/6)- or poly adenosine diphosphate-ribose polymerase (PARP)- inhibitor
- Must have an increased risk of disease recurrence based on clinical-pathological risk features
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate organ function

### KEY EXCLUSION CRITERIA

- Any evidence of metastatic disease (including contralateral axillary lymph node [ALN]) or inflammatory breast cancer at primary breast cancer diagnosis
- Greater than a 6-month consecutive gap in therapy during prior adjuvant ET
- Participants who have completed or discontinued prior adjuvant ET >6 months prior to screening
- History of previous breast cancer are excluded, except for ipsilateral ductal carcinoma *in situ* (DCIS) treated by locoregional therapy alone  $\geq$ 5 years ago
- Pregnant, breastfeeding, or expecting to conceive or father children within the projected duration of the trial, starting with the screening visit through 180 days after the last dose of study intervention
- Prior ET of any duration for breast cancer prevention (tamoxifen or aromatase inhibitors [AIs]) or raloxifene
- History of any other cancer
- Serious preexisting medical conditions

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT05514054].

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## ACTIVE TRIALS CURRENTLY NOT ENROLLING

### **[NCT04188548] Breast Cancer**

EMBER: A Study of LY3484356 for Patients With ER+, Locally Advanced or Metastatic Breast Cancer and Other Select Non-Breast Cancers

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Pipeline information is current through February 6, 2024.