The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.
TARGET
Estrogen signaling plays an important role in organ development and growth. In certain cancers, abnormal estrogen signaling via the estrogen receptor is a key component of tumor growth. 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 has demonstrated the inhibition of estrogen signaling and subsequent inhibition of cell proliferation in ER-expressing tumor models.

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

References:

The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.
A Phase 1a/1b Study of LY3484356 Administered as Monotherapy and in Combination With Anticancer Therapies for Patients With ER+, Locally Advanced or Metastatic Breast Cancer and Other Select Non-breast Cancers*

The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.

**KEY INCLUSION CRITERIA**

- All study parts:
  - Willing to provide adequate archival tissue sample
  - Willing to use highly effective birth control
  - Adequate organ function
  - Able to swallow capsules
- Participants must have one of the following (dose escalation):
  - Parts A and B: Estrogen-receptor-positive (ER+), HER2-negative breast cancer with evidence of locally advanced, unresectable or metastatic disease and have had the following:
    - Part A: May have had up to one prior regimen of any kind in the advanced/metastatic setting and no prior CDK4 & 6 inhibitor therapy
    - Part B: May have had up to two prior regimens; no more than one of which may be endocrine therapy in the advanced/metastatic setting, and must have received a prior CDK4 & 6 inhibitor
  - Cohort E4: No prior everolimus
  - Cohort E5: No prior alpelisib and must have a phosphatidylinositol 3-kinase catalytic α (PIK3Cα) mutation as determined by local testing
  - Part C: ER+, HER2-positive breast cancer with evidence of locally advanced, unresectable or metastatic disease who have had at least 2 HER2-directed therapies in any setting
  - Part D: ER+, EEC that has progressed after platinum-containing chemotherapy and no prior fulvestrant or aromatase inhibitor therapy
  - Part E: ER+ and HER2-positive breast cancer with evidence of locally advanced, unresectable, or metastatic disease

- Part E: Participants must have received induction taxane chemotherapy combined with trastuzumab + pertuzumab as first-line treatment for advanced/metastatic disease and must not have progressed on this regimen
- Part E: Participants must not have received more than one HER2-directed regimen or any endocrine therapy for advanced disease or any prior CDK4 & 6 inhibitor therapy
- Participants with ER+, HER2-negative breast cancer enrolled in this study must have evidence of clinical benefit while on endocrine therapy for at least 24 months in the adjuvant setting or at least 6 months in the advanced/metastatic setting, or have untreated de novo metastatic breast cancer

**KEY EXCLUSION CRITERIA**

- Uncontrolled infections such as hepatitis, tuberculosis, or HIV
- Another serious medical condition
- Unstable cancer of the central nervous system
- Pregnant or breastfeeding

---

* This clinical trial is being conducted globally.
† LY3484356 is administered PO QD.
‡ Abemaciclib is administered PO BID.
§ Aromatase inhibitor (AI) is administered PO.
|| Everolimus is administered PO QD.
¶ Alpelisib is administered PO QD.
# Trastuzumab is administered intravenously (IV) Q21D.
** Pertuzumab is administered IV Q21D.

Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT04188548].
The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.
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*

The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.

**KEY INCLUSION CRITERIA**

- Diagnosis of estrogen-receptor-positive (ER+), HER2-negative (HER2-) early-stage, resected, invasive breast cancer without evidence of distant metastases
- 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 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 ≥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

**Imlunestrant**

Primary endpoint: Invasive disease-free survival (excluding second non-breast primary invasive cancer)

**Tamoxifen, anastrozole, letrozole, or exemestane**

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

---

* This clinical trial is being conducted globally.
† Imlunestrant is administered PO.
‡ Endocrine therapy. Investigator’s choice of tamoxifen, anastrozole, letrozole or exemestane is administered per local approved label.
The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.
ACTIVE TRIALS CURRENTLY NOT ENROLLING

[NCT04647487] Breast Cancer
EMBER-2: A Study Evaluating LY3484356 in Postmenopausal Women With Stage I-III, Estrogen-Receptor-Positive, HER2-Negative Breast Cancer