For Healthcare Professionals

About the ReDiscover-2 Study

Study Purpose

The purpose of the ReDiscover-2 Study is to assess the efficacy and safety of RLY-2608 + fulvestrant versus capivasertib + fulvestrant as treatment for *PIK3CA*-mutant HR+/HER2- locally advanced or metastatic breast cancer following recurrence or progression on or after treatment with a CDK4/6 inhibitor.

Study Design

This is a phase 3, open-label, randomized study that is enrolling approximately 540 participants globally to receive either RLY-2608 in combination with fulvestrant or capivasertib in combination with fulvestrant.

The total duration of participation will vary for each participant but may last from several months to 1 year or longer. The study includes a screening period (up to 28 days), treatment period (ongoing 28-day cycles), and a follow-up period (ongoing). Participants will attend 1–2 visits per treatment period cycle and then regular follow-up visits.

The investigational study drug, RLY-2608, is an oral capsule taken twice daily. Capivasertib is an oral tablet that will be taken twice daily for 4 days followed by 3 days off every week. Fulvestrant will be administered at the study site as two injections occurring twice in the first cycle, then once per cycle thereafter.

Refer a Patient

If you have a patient who may be eligible for this study, please contact the research site listed here for more information. The study team can answer any questions about the study. You can also visit **clinicaltrials.gov** (NCT06982521).

Each potential participant will be required to have a screening visit with the study doctor to see if they qualify. Those who do qualify and enroll will receive the study drugs (RLY-2608 and fulvestrant or capivasertib and fulvestrant) and study-related care at no cost to them or their families. Any patients you refer to this study will be seen for study-related reasons only.

The research site closest to you is:

Key Eligibility Criteria

Inclusion

- ≥ 18 years of age
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
- Female participants may be postmenopausal, perimenopausal, or premenopausal
- Histologically or cytologically confirmed diagnosis of locally advanced or metastatic adenocarcinoma of the breast with radiological or objective evidence of recurrence or progression; locally advanced disease must not be amenable to resection with curative intent (participants who are considered suitable for surgical or ablative techniques following potential down-staging with study treatment are not eligible)
- One or more known primary oncogenic *PIK3CA* mutation(s) in tissue or blood documented per validated local assessment and confirmed by central testing
- Radiological evidence of progression on or after previous treatment for HR+/HER2- advanced breast cancer (ABC) with:
  - At least 1 and no more than 2 lines of endocrine therapy (ET) (single agent or in combination)
    AND
  - One prior line of CDK4/6 inhibitor therapy
- No more than 1 prior line of chemotherapy in the ABC setting

Exclusion

- Metaplastic or inflammatory breast cancer
- Type 1 diabetes, type 2 diabetes requiring antihyperglycemic medication, or fasting plasma glucose ≥ 140 mg/dL, or HbA1c ≥ 7.0% (≥ 53 mmol/mol)
- Prior treatment with any of the following:
  - CDK2 or selective CDK4 inhibitors or any investigational therapies targeting CDKs
  - PI3K, AKT, or mTOR inhibitors, or any agent whose mechanism of action is to inhibit the PI3K/AKT/mTOR pathway
  - Immunotherapy
  - Antibody drug conjugates
- Prior treatment with > 2 lines of ET for ABC
- Known activating AKT mutations, loss-of-function PTEN mutations, or loss of PTEN expression resulting in oncogenic pathway activation downstream of PI3K

Additional eligibility criteria, according to approved protocol, will apply.

ReDiscover-2 STUDY

RELAY THERAPEUTICS