

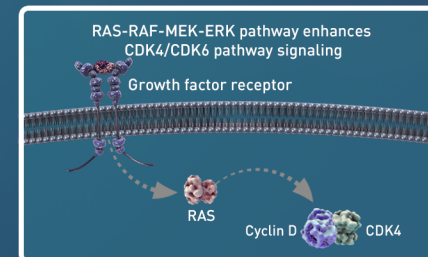
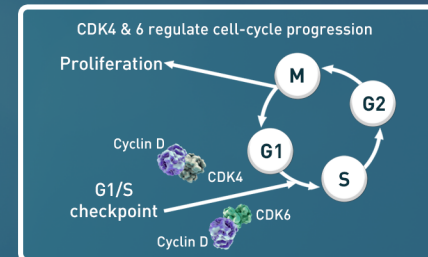
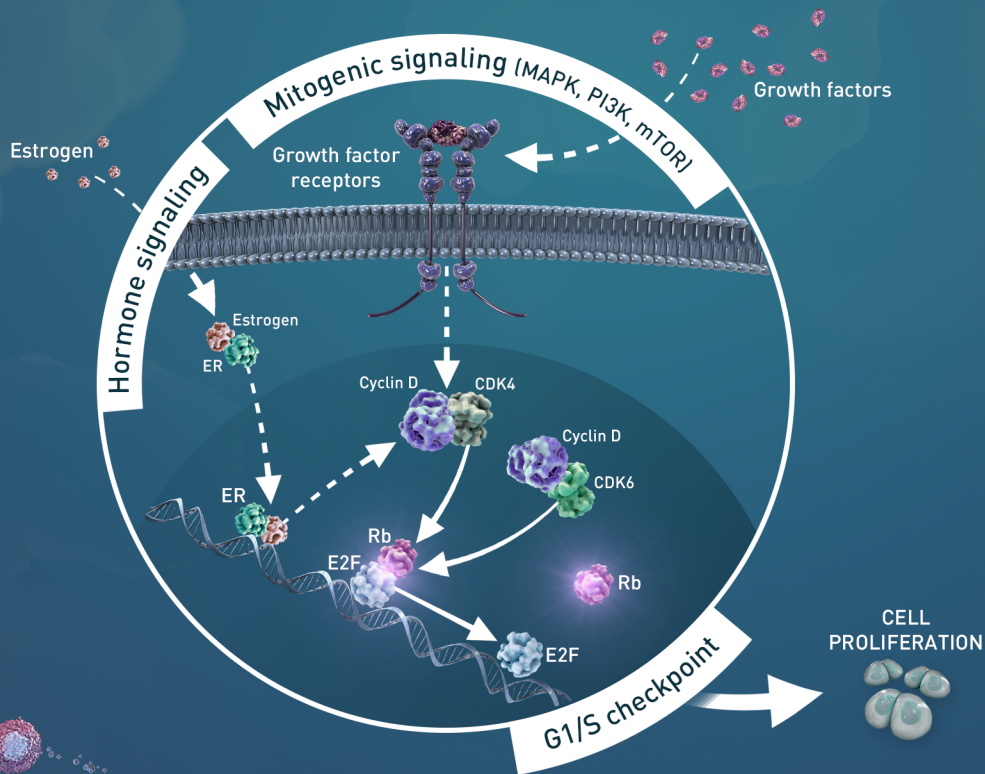
# ABEMACICLIB

## CDK4/6 INHIBITOR

The safety and efficacy of the agents for uses under investigation have not been established. Pipeline molecules may not receive regulatory approval and become commercially available for the uses being investigated. The information provided about new molecules being studied is for scientific information exchange purposes only with no commercial intent. For more information on our pipeline, please visit [lillyloxooncologypipeline.com](https://lillyloxooncologypipeline.com).

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# ABEMACICLIB | MECHANISM OF ACTION<sup>1</sup>



Reference: 1. Shapiro GI. *J Clin Oncol*. 2006;24(11):1770-1783.

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## TARGET

Many human tumors acquire alterations which can lead to the activation of cyclin-dependent kinases (CDKs). These alterations include mutations that directly activate CDK4/6; gene amplifications, which increase expression of various protein activators such as D-type cyclins; as well as genetic losses, which reduce expression of protein inhibitors such as p16. These various mechanisms as well as loss of retinoblastoma (Rb) can lead to an enhanced proliferative potential by decreasing dependency on external growth factors and mitogenic signaling pathways, which are required to stimulate growth under normal conditions.<sup>1,2</sup>

## MOLECULE

Abemaciclib has been shown in vitro to be a selective ATP-competitive inhibitor of CDK4/6 kinase activity that prevents the phosphorylation and subsequent inactivation of the Rb tumor suppressor protein, thereby inducing G1 cell-cycle arrest and inhibition of cell proliferation.<sup>3,4</sup>

## CLINICAL DEVELOPMENT

Abemaciclib is being investigated in clinical trials in patients with breast cancer, non-small cell lung cancer, pediatric cancers, prostate cancer, or sarcoma.

**References:** **1.** Kim JK, Diehl JA. *J Cell Physiol.* 2009;220(2):292-296. **2.** Choi YJ, Anders L. *Oncogene.* 2014;33(15):1890-1903. **3.** Dempsey JA, et al. AACR Annual Meeting; April 6-10, 2013; Washington, DC. Abstract LB122. **4.** Gelbert LM, et al. *Invest New Drugs.* 2014;32(5):825-837.

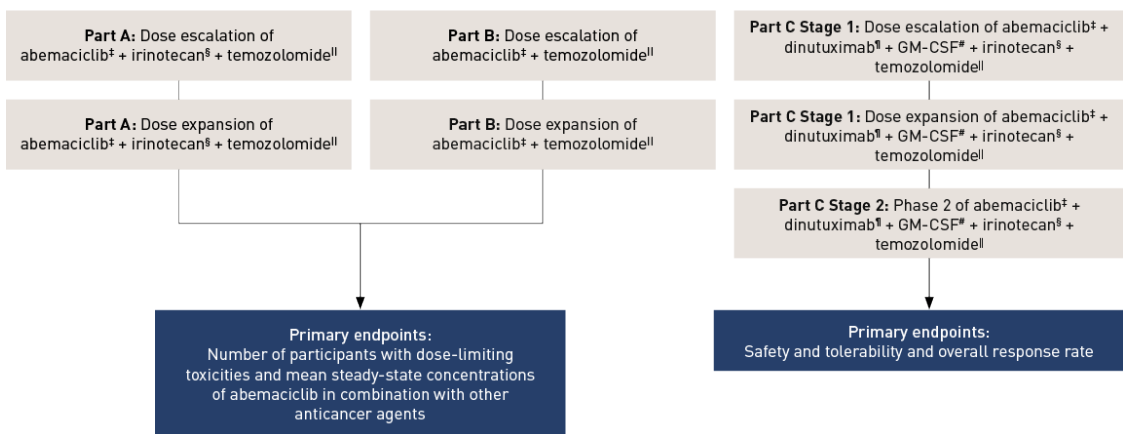
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**NCT04238819**

**A Phase 1b/2 Study of Abemaciclib in Combination With Irinotecan and Temozolomide (Part A) and Abemaciclib in Combination With Temozolomide (Part B) in Pediatric and Young Adult Patients With Relapsed/Refractory Solid Tumors and Abemaciclib in Combination With Dinutuximab, GM-CSF, Irinotecan, and Temozolomide in Pediatric and Young Adult Patients With Relapsed/Refractory Neuroblastoma (Part C)\*\***



\* This clinical trial is being conducted globally.  
 † Additional criteria not shown here may exist for individual parts of the study.  
 ‡ Abemaciclib is administered PO.  
 § Irinotecan is administered intravenously (IV).  
 || Temozolomide is administered PO or IV.  
 ¶ Dinutuximab is administered IV.  
 # GM-CSF is administered subcutaneously.

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT04238819].

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NCT04238819

**A Phase 1b/2 Study of Abemaciclib in Combination With Irinotecan and Temozolomide (Part A) and Abemaciclib in Combination With Temozolomide (Part B) in Pediatric and Young Adult Patients With Relapsed/Refractory Solid Tumors and Abemaciclib in Combination With Dinutuximab, GM-CSF, Irinotecan, and Temozolomide in Pediatric and Young Adult Patients With Relapsed/Refractory Neuroblastoma (Part C) (cont.)**

## KEY INCLUSION CRITERIA

Parts A and B only:

- ≤18 years of age
- Body weight ≥10 kilograms and body surface area (BSA) ≥0.5 m<sup>2</sup>
- Any relapsed/refractory malignant solid tumor (excluding lymphoma), including central nervous system tumors, that have progressed on standard therapies
- For parts B and C, participants with neuroblastoma who are eligible for part C will be excluded from part B unless approved by the investigator

Part C only:

- <21 years of age
- BSA ≥0.2 m<sup>2</sup>
- First relapse/refractory neuroblastoma

All parts:

- Measurable or evaluable disease as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 or Response Assessment in Neuro-Oncology (RANO)
- A Lansky score ≥50 for participants <16 years of age or Karnofsky score ≥50 for participants ≥16 years of age

- Discontinued all previous treatments for cancer or investigational agents and recovered from the acute effects to grade ≤1 at the time of enrollment
- Able to swallow and/or have a gastric/nasogastric tube
- Adequate hematologic and organ function ≤2 weeks (14 days) prior to first dose of study treatment
- Females of reproductive potential must have negative urine or serum pregnancy test at baseline (within 7 days prior to starting treatment)
- Female participants of reproductive potential must agree to use highly effective contraceptive precautions during the trial. For abemaciclib, females should use contraception for at least 3 weeks following the last abemaciclib. For other study drugs, highly effective contraceptive precautions (and avoiding sperm donation) must be used according to their label
- Life expectancy of at least 8 weeks and able to complete at least 1 cycle of treatment
- Caregivers and participants willing to make themselves available for the duration of the trial

## KEY EXCLUSION CRITERIA

- Prior allogenic bone marrow or solid organ transplant
- Prior live vaccination
- Intolerability or hypersensitivity to any of the study treatments or its components
- Diagnosed and/or treated additional malignancy within 3 years prior to enrollment that may affect the interpretation of results, with the exception of curatively treated basal cell carcinoma of the skin, squamous cell carcinoma of the skin, and/or curatively resected in situ cervical and/or breast cancers
- Pregnant or breastfeeding
- Active systemic infections
- Serious and/or uncontrolled preexisting medical condition(s)
- Parts A and C only: Bowel obstruction
- Prior treatment with drugs known to be strong inhibitors or inducers of isoenzyme cytochrome P450 3A (CYP3A) or strong inhibitors of uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1) if the treatment cannot be discontinued or switched to a different medication at least 5 half-lives prior to starting study treatment
- Prior treatment with cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor
- Part C only: Received prior systemic therapy for relapsed/refractory neuroblastoma
- Part C only: Received prior anti-GD2 therapy during induction phase
- Currently enrolled in any other clinical study involving an investigational product or non-approved use of a drug or device
- Received an experimental treatment in a clinical trial within the last 30 days or 5 half-lives, whichever is longer

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT04238819].

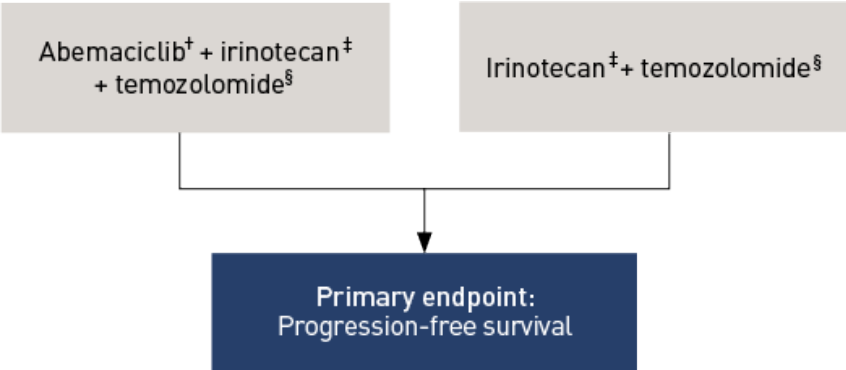
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CAMPFIRE

A Randomized, Open-Label, Phase 2 Study Evaluating Abemaciclib in Combination With Irinotecan and Temozolomide in Participants With Relapsed or Refractory Ewing’s Sarcoma\*



\* This clinical trial is being conducted globally.  
† Abemaciclib is administered PO.  
‡ Irinotecan is administered intravenously.  
§ Temozolomide is administered PO.

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT05440786].

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## CAMPFIRE

### A Randomized, Open-Label, Phase 2 Study Evaluating Abemaciclib in Combination With Irinotecan and Temozolomide in Participants With Relapsed or Refractory Ewing's Sarcoma (cont.)

#### KEY INCLUSION CRITERIA

- Ages 1 to 39
- Ewing's sarcoma or Ewing's sarcoma-like tumor
  - The original pathological report is required; repeat biopsy at progression is not required
- Refractory disease or confirmed radiological progression or recurrence following first or later line of treatment of Ewing's sarcoma or Ewing's sarcoma-like tumor
  - Participants must have one measurable or evaluable lesion as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Lansky score  $\geq 50$  for participants <16 years of age, and Karnofsky score  $\geq 50$  for participants  $\geq 16$  years of age
- Participants must have discontinued all previous treatments for cancer or investigational agents  $\geq 7$  days after the last dose and must have recovered from the acute effects
- Adequate hematologic and organ function  $\leq 14$  days prior to day 1 of cycle 1
  - Platelets  $\geq 75 \times 10^9/L$ , hemoglobin  $\geq 8$  g/dL, and absolute neutrophil count  $\geq 1.0 \times 10^9/L$
  - Aspartate aminotransferase (AST) and alanine aminotransferase (ALT)  $\leq 3.0 \times$  upper limit of normal (ULN); total bilirubin  $\leq 1.5 \times$  ULN
  - Creatinine clearance or calculated glomerular filtration rate (GFR)  $\geq 60$  mL/min/m<sup>2</sup> or serum creatinine based on age/gender
- Female participants of childbearing potential must have a negative urine or serum pregnancy test
- Body weight  $\geq 10$  kg
- Must be able to swallow and/or have a gastric/nasogastric tube
  - Participants in the European Union must be able to swallow intact capsules
- Stable or decreasing dose of steroids at least 7 days prior to enrollment
- Life expectancy of at least 8 weeks and able to complete at least 1 cycle of treatment
- Participants/caregivers are willing to follow study procedures and make themselves available for the duration of the study

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT05440786].

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#### KEY EXCLUSION CRITERIA

- Severe and/or uncontrolled concurrent medical disease or psychiatric illness/social situation that, in the judgment of the investigator, could cause unacceptable safety risks or compromise compliance with the protocol
- Active fungal, bacterial, and/or known severe viral infection, including but not limited to HIV or viral hepatitis A, B, or C
- Prior allogeneic bone marrow or solid organ transplant
- Major surgical procedure, laparoscopic procedure, or significant traumatic injury within 28 days prior to enrollment. Surgical or other wounds must be adequately healed prior to enrollment
- Pregnant or breastfeeding
- Prior treatment with a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor
- Progression during prior treatment with irinotecan and/or temozolomide
- Known intolerance or hypersensitivity to any of the study treatments or dacarbazine
- Diagnosed and/or treated for an additional malignancy within 3 years prior to enrollment

## ACTIVE TRIALS CURRENTLY NOT ENROLLING

### **[NCT02057133] Breast Cancer**

A Study of LY2835219 (Abemaciclib) in Combination With Therapies for Breast Cancer That Has Spread

### **[NCT02107703] Breast Cancer**

MONARCH 2: A Study of Abemaciclib (LY2835219) Combined With Fulvestrant in Women With Hormone-Receptor-Positive, HER2-Negative Breast Cancer

### **[NCT02246621] Breast Cancer**

MONARCH 3: A Study of Nonsteroidal Aromatase Inhibitors Plus Abemaciclib (LY2835219) in Postmenopausal Women With Breast Cancer

### **[NCT02675231] Breast Cancer**

monarchHER: A Study of Abemaciclib (LY2835219) in Women With HR+, HER2+ Locally Advanced or Metastatic Breast Cancer

### **[NCT02779751] Lung Cancer or Breast Cancer**

A Study of Abemaciclib (LY2835219) in Participants With Non-Small Cell Lung Cancer or Breast Cancer

### **[NCT02747004] Breast Cancer**

Next MONARCH 1: A Study of Abemaciclib (LY2835219) Plus Tamoxifen or Abemaciclib Alone in Women With Metastatic Breast Cancer

### **[NCT02763566] Breast Cancer**

MONARCH plus: A Study of Abemaciclib (LY2835219) in Participants With Breast Cancer

### **[NCT03155997] Breast Cancer**

monarchE: Endocrine Therapy With or Without Abemaciclib (LY2835219) Following Surgery in Participants With Breast Cancer

### **[NCT05169567] Breast Cancer**

postMONARCH: Abemaciclib (LY2835219) Plus Fulvestrant Compared to Placebo Plus Fulvestrant in Previously Treated Breast Cancer

### **[NCT03703466] Breast Cancer**

A Study of Abemaciclib (LY2835219) With and Without Food in Participants With Metastatic Breast Cancer

### **[NCT05999968] Prostate Cancer**

Abemaciclib Plus Darolutamide in Prostate Cancer That Has Spread After Initial Treatment

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Pipeline information is current through February 6, 2024.

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