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

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.1,2

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.3,4

CLINICAL DEVELOPMENT

Abemaciclib is being investigated in clinical trials in patients with breast cancer, pediatric cancer, or prostate 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 Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Compare the Efficacy of Abemaciclib Plus Fulvestrant to Placebo Plus Fulvestrant in Participants With HR+, HER2-, Advanced or Metastatic Breast Cancer Following Progression on a CDK4 & 6 Inhibitor and Endocrine Therapy*

* This clinical trial is being conducted globally.
† Abemaciclib or placebo equivalent is administered PO.
‡ Fulvestrant is administered intramuscularly.

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.

Primary endpoint: Progression-free survival

**postMONARCH**

**KEY INCLUSION CRITERIA**

- Hormone-receptor-positive (HR+), HER2-negative (HER2-) locally advanced or metastatic breast cancer
- Radiographic evidence of disease progression or recurrence either:
  - On treatment with a CDK4 & 6 inhibitor with aromatase inhibitor (AI) as initial therapy for advanced disease, or
  - On/after treatment with a CDK4 & 6 inhibitor plus endocrine therapy (ET) administered as adjuvant therapy for early-stage breast cancer
- Must be deemed appropriate for treatment with ET
- If female, have a postmenopausal status by natural or surgical means or by ovarian function suppression
- Measurable disease and/or nonmeasurable disease as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate renal, hematologic, and hepatic organ function
- Able to swallow capsules/tablets

**KEY EXCLUSION CRITERIA**

- Visceral crisis, lymphangitic spread, or leptomeningeal carcinomatosis
- Symptomatic or untreated central nervous system metastasis
- Received any systemic therapy between disease recurrence/progression and study screening
- Received more than one line of therapy for advanced or metastatic disease
- Prior chemotherapy for metastatic breast cancer (MBC)
- Prior treatment with fulvestrant, any investigational estrogen receptor (ER)-directed therapy (including selective ER degraders [SERDs] and non-SERDs), any PI3K, mTOR, or AKT inhibitor
- Hormone-receptor-positive (HR+), HER2-negative (HER2-) locally advanced or metastatic breast cancer
- Radiologic evidence of disease progression or recurrence either:
  - On treatment with a CDK4 & 6 inhibitor with aromatase inhibitor (AI) as initial therapy for advanced disease, or
  - On/after treatment with a CDK4 & 6 inhibitor plus endocrine therapy (ET) administered as adjuvant therapy for early-stage breast cancer
- Must be deemed appropriate for treatment with ET
- If female, have a postmenopausal status by natural or surgical means or by ovarian function suppression
- Measurable disease and/or nonmeasurable disease as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate renal, hematologic, and hepatic organ function
- Able to swallow capsules/tablets

Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT05169567].
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**

- Metastatic prostate cancer documented by positive bone scan and/or measurable soft tissue metastatic lesions by CT or MRI
- Progressive disease at study entry demonstrated during continuous androgen-deprivation therapy (ADT)/post orchiectomy defined as one or more of the following:
  - Prostate-specific antigen (PSA) progression
  - Radiographic progression as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 for soft tissue and/or per Prostate Cancer Working Group 3 (PCWG3) for bone, with or without PSA progression
- Adequate organ function
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

**KEY EXCLUSION CRITERIA**

- Prior therapy with cytochrome P450 (CYP)17 inhibitors
- Prior treatment with abemaciclib or any cyclin-dependent kinase (CDK) 4 & 6 inhibitors
- Prior cytotoxic chemotherapy for metastatic castration-resistant prostate cancer (participants treated with docetaxel for metastatic hormone-sensitive prostate cancer [mHSPC] are eligible). Prior radiopharmaceuticals for prostate cancer, or prior enzalutamide, apalutamide, darolutamide, or sipuleucel-T. Participants who had prior radiation or surgery to all target lesions
- Currently enrolled in a clinical study involving an investigational product
- Gastrointestinal disorder affecting the absorption or ability to swallow large pills
- Clinically significant heart disease, active or chronic liver disease, moderate/severe hepatic impairment (Child-Pugh Class B and C)

Please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov) for more information on this clinical trial [NCT03706365].

**CYCLONE 2**

A Phase 2/3, Randomized, Double-Blind, Placebo-Controlled Study of Abiraterone Acetate Plus PrednisoneWith or Without Abemaciclib in Patients With Metastatic Castration-Resistant Prostate Cancer*

* This clinical trial is being conducted globally.
† Abiraterone, prednisone (or prednisolone), and abemaciclib or placebo equivalent are administered PO.

**Primary endpoint:** Radiographic progression-free survival
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**

- Adenocarcinoma of the prostate (as the predominant histology)
- High-risk metastatic hormone-sensitive prostate cancer. High risk is defined as: ≥4 bone metastases by bone scan and/or ≥1 visceral metastases by CT or MRI
- Must have initiated androgen deprivation therapy (ADT) with luteinizing hormone-releasing hormone (LHRH) agonist/antagonist or bilateral orchiectomy prior to randomization. Up to 3 months of ADT prior to randomization is permitted with or without first-generation anti-androgen
- Adequate organ function
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

**KEY EXCLUSION CRITERIA**

- Prior treatment with abemaciclib or any other CDK4 & 6 inhibitor
- Development of metastatic prostate cancer in the context of castrate levels of testosterone
- Received any prior systemic therapy for metastatic prostate cancer (including investigational agents), except for ADT and first-generation anti-androgen
- Clinically significant cardiovascular disease as evidenced by myocardial infarction, arterial thrombotic events, or severe/unstable angina in the past 6 months, or New York Heart Association Class II to IV heart failure
- History of syncope of cardiovascular etiology, ventricular arrhythmia of pathological origin, or sudden cardiac arrest. Chronic and hemodynamically stable atrial arrhythmia well-controlled on medical therapy is permitted
- Uncontrolled hypertension
- Clinically active or chronic liver disease, moderate/severe hepatic impairment
- Known untreated central nervous system (CNS) metastasis. Patients with a history of treated brain metastases are eligible if stable for at least 8 weeks prior to randomization and off corticosteroid for at least 2 weeks prior to randomization

Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT05288166].

**CYCLONE 3**

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Abemaciclib in Combination With Abiraterone Plus Prednisone in Men With High-Risk Metastatic Hormone-Sensitive Prostate Cancer*

* This clinical trial is being conducted globally.
† Abiraterone, prednisone (or prednisolone), and abemaciclib or placebo equivalent are administered PO.
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)‡

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.

Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT04238819].

* 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).
¶ Dinutuximab is administered IV.
# GM-CSF is administered subcutaneously.

**KEY INCLUSION CRITERIA**

Parts A and B only:
• ≤18 years of age
• Body weight ≥30 kilograms and body surface area (BSA) ≥0.5 m²
• Any relapsed/refractory malignant solid tumor (excluding lymphoma), excluding 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 ≥0.3 m²
• 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
• Adequate hematologic and organ function
• Females of reproductive potential must have negative urine or serum pregnancy test at baseline (within 7 days prior to starting treatment)
• participant’s female 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.
• 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
• Irinotecan 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 or viral load
• 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 (CDK) 4 & 6 inhibitor
• Part C only: Received prior systemic therapy for relapsed/refractory neuroblastoma
• 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
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.

Primary endpoint: Progression-free survival

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  
- Confirmed radiological progression or refractory disease  
- Participants must have one measurable or evaluable lesion as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1  
- Lansky score ≥50 for participants <16 years of age, and Karnofsky score ≥50 for participants ≥16 years of age  
- Participants must have discontinued all previous treatments for cancer or investigational agents ≥7 days after the last dose and must have recovered from the acute effects  
- Adequate hematologic and organ function ≤14 days prior to day 1 of cycle 1  
- Platelets ≥75 x 10^9/L, hemoglobin ≥8 g/dL, and absolute neutrophil count ≥1.0 x 10^9/L  
- Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤3.0 x upper limit of normal (ULN); total bilirubin ≤1.5 x ULN  
- Creatinine clearance or calculated glomerular filtration rate (GFR) ≥60 mL/min/m² or serum creatinine based on age/gender  
- Female participants of childbearing potential must have a negative urine or serum pregnancy test  
- Male participants must agree to use adequate contraception for the duration of the study or until completion of 90 days after study treatment discontinuation  
- Body weight ≥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  
- Participants/caregivers are willing to follow study procedures and make themselves available for the duration of the study

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 CDK4 & 6 inhibitor  
- Progression during prior treatment with irinotecan or temozolomide  
- Known intolerability or hypersensitivity to any of the study treatments or dacarbazine  
- Diagnosed and/or treated for an additional malignancy within 3 years prior to enrollment  
- 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  
- Confirmed radiological progression or refractory disease  
- Participants must have one measurable or evaluable lesion as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1  
- Lansky score ≥50 for participants <16 years of age, and Karnofsky score ≥50 for participants ≥16 years of age  
- Participants must have discontinued all previous treatments for cancer or investigational agents ≥7 days after the last dose and must have recovered from the acute effects  
- Adequate hematologic and organ function ≤14 days prior to day 1 of cycle 1  
- Platelets ≥75 x 10^9/L, hemoglobin ≥8 g/dL, and absolute neutrophil count ≥1.0 x 10^9/L  
- Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤3.0 x upper limit of normal (ULN); total bilirubin ≤1.5 x ULN  
- Creatinine clearance or calculated glomerular filtration rate (GFR) ≥60 mL/min/m² or serum creatinine based on age/gender  
- Female participants of childbearing potential must have a negative urine or serum pregnancy test  
- Male participants must agree to use adequate contraception for the duration of the study or until completion of 90 days after study treatment discontinuation  
- Body weight ≥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  
- Participants/caregivers are willing to follow study procedures and make themselves available for the duration of the study  
- 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  
- Confirmed radiological progression or refractory disease  
- Participants must have one measurable or evaluable lesion as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1  
- Lansky score ≥50 for participants <16 years of age, and Karnofsky score ≥50 for participants ≥16 years of age  
- Participants must have discontinued all previous treatments for cancer or investigational agents ≥7 days after the last dose and must have recovered from the acute effects  
- Adequate hematologic and organ function ≤14 days prior to day 1 of cycle 1  
- Platelets ≥75 x 10^9/L, hemoglobin ≥8 g/dL, and absolute neutrophil count ≥1.0 x 10^9/L  
- Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤3.0 x upper limit of normal (ULN); total bilirubin ≤1.5 x ULN  
- Creatinine clearance or calculated glomerular filtration rate (GFR) ≥60 mL/min/m² or serum creatinine based on age/gender  
- Female participants of childbearing potential must have a negative urine or serum pregnancy test  
- Male participants must agree to use adequate contraception for the duration of the study or until completion of 90 days after study treatment discontinuation  
- Body weight ≥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  
- Participants/caregivers are willing to follow study procedures and make themselves available for the duration of the study
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

[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
monarcHER: A Study of Abemaciclib (LY2835219) in Women With HR+, HER2+ Locally Advanced or Metastatic 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

[NCT03703466] Breast Cancer
A Study of Abemaciclib (LY2835219) With and Without Food in Participants With Metastatic Breast Cancer

[NCT04408924] Prostate Cancer
CYCLONE 1: A Study of Abemaciclib in Metastatic Castration-Resistant Prostate Cancer Patients