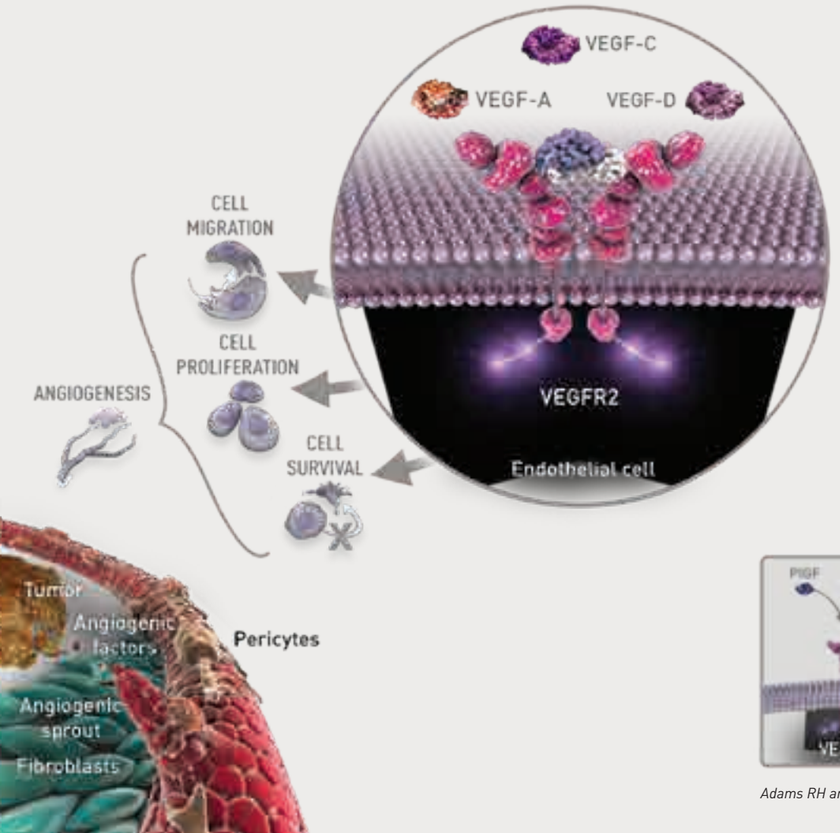
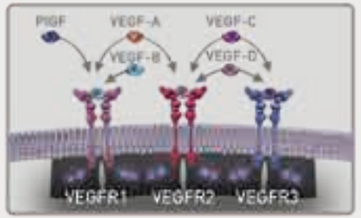
# RAMUCIRUMAB

## VEGF RECEPTOR-2 ANTAGONIST

Lilly

***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.***




*Adams RH and Alitalo K[1]; Hicklin DJ and Ellis LM[2]*

## TARGET

Angiogenesis is a tightly regulated, multiple-step process, which results in the formation of new blood vessels from preexisting vasculature and is an important component in the development and progression of malignant disease. Signaling by vascular endothelial growth factor (VEGF) receptor-2 in endothelial cells plays a role in inducing normal and pathologic angiogenesis and is activated by binding of ligands VEGF-A, VEGF-C, and VEGF-D.[1-3]

## MOLECULE

Ramucirumab is a human IgG1 monoclonal antibody receptor antagonist that has been shown in vitro to bind to and block the activation of VEGF receptor-2 by preventing the binding of VEGF receptor ligands VEGF-A, VEGF-C, and VEGF-D.[4,5]

## CLINICAL DEVELOPMENT

Ramucirumab is being investigated in clinical trials in patients with non-small cell lung cancer or pediatric sarcoma.

**References: 1.** Adams RH, Alitalo K. *Nat Rev Mol Cell Biol.* 2007;8(6):464-478. **2.** Hicklin DJ, Ellis LM. *J Clin Oncol.* 2005;23(5):1011-1027. **3.** Olsson AK, et al. *Nat Rev Mol Cell Biol.* 2006;7(5):359-371. **4.** Lu D, et al. *J Biol Chem.* 2003;278(44):43496-43507. **5.** Zhu Z, et al. *Leukemia.* 2003;17(3):604-611.

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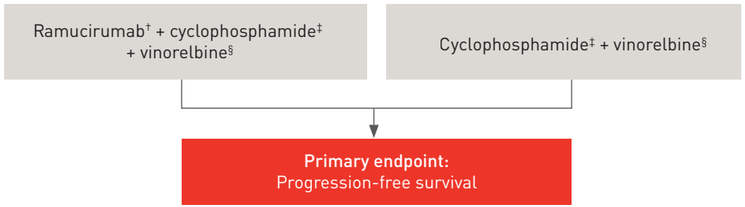
## CAMPFIRE

A Randomized, Open-Label Phase 1/2 Study Evaluating Ramucirumab in Pediatric Patients and Young Adults With Relapsed, Recurrent, or Refractory Desmoplastic Small Round Cell Tumor*

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* This clinical trial is being conducted globally.
† Ramucirumab is administered intravenously (IV).
‡ Cyclophosphamide is administered PO.
§ Vinorelbine is administered IV.
|| Additional criteria apply.



## KEY INCLUSION CRITERIA

- If in the US, aged 12 months to 29 years. If in the EU, aged 36 months to 29 years and >11 kg at study entry
- Relapsed, recurrent, or refractory desmoplastic small round cell tumors
- Measurable disease as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Received at least one prior line of systemic treatment (including neoadjuvant/adjuvant chemotherapy), including approved therapies for which the patient is eligible
- Discontinued all previous treatments for cancer or investigational agents ≥7 days prior to study entry and recovered from select acute effects to grade ≤2 for alopecia and decreased tendon reflex, and to grade ≤1 for all other effects at the time of enrollment||
- Adequate hematologic and organ function for at least 7 days prior to first dose of study drug||
- Female participants of childbearing potential must have a negative urine or serum pregnancy test within 7 days prior to randomization. Male and female participants must agree to use highly effective contraception for the duration of the study and up to 3 months following the last dose of ramucirumab and vinorelbine, and 12 months following the last dose of cyclophosphamide

## KEY EXCLUSION CRITERIA

- Eligible for surgical resection at time of enrollment
- Active infections requiring therapy, including HIV or hepatitis A, B, or C
- Prior allogeneic bone marrow or solid organ transplant
- Major surgical, laparoscopic, or significant traumatic injury within 28 days prior to enrollment. Surgical or other wounds must be adequately healed prior to enrollment
- Evidence of active bleeding, a bleeding diathesis or vasculitis, or a history of significant (grade ≥3) bleeding event, hemoptysis or pulmonary hemorrhage, a DVT or PE requiring medical intervention, or esophageal varices within 3 months prior to enrollment
- History of central nervous system arterial/venous thromboembolic events, including transient ischemic attack or cerebrovascular accident within 6 months prior to study enrollment, myocardial infarction or unstable angina within the prior 6 months, New York Heart Association (NYHA) grade ≥2 congestive heart failure, serious and inadequately controlled cardiac arrhythmia, significant vascular disease, or clinically significant peripheral vascular disease
- History of fistula, gastrointestinal ulcer or perforation, or intra-abdominal abscess within 3 months of study enrollment
- History of hypertensive crisis or hypertensive encephalopathy within 6 months of study enrollment
- Known hypersensitivity to ramucirumab, cyclophosphamide, vinorelbine, or any of the excipients of the medicinal product
- Severe liver cirrhosis (Child-Pugh class B or worse), cirrhosis with a history of hepatic encephalopathy, clinically meaningful ascites resulting from cirrhosis and requiring ongoing treatment with diuretics and/or paracentesis, or history of hepatorenal syndrome
- Bowel obstruction, history or presence of inflammatory enteropathy or extensive intestinal resection, Crohn's disease, ulcerative colitis, or chronic diarrhea
- Urinary outflow obstruction, grade 2 hematuria, or noninfectious cystitis at the time of screening
- Severe and/or uncontrolled concurrent medical disease or psychiatric illness/social situation that, in the opinion of the investigator, could cause unacceptable safety risks or compromise protocol compliance
- Prior treatment with/progression on combination cyclophosphamide and vinorelbine regimen; prior treatment with ramucirumab

**Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT04145349].**

## ACTIVE TRIALS CURRENTLY NOT ENROLLING

**[NCT02411448] Lung Cancer**
RELAY: A Study of Ramucirumab (LY3009806) in Combination With Erlotinib in Participants With EGFR Mutation-Positive Metastatic NSCLC

**[NCT02789345] Lung Cancer**
A Study of Ramucirumab (LY3009806) or Necitumumab (LY3012211) Plus Osimertinib in Participants With Lung Cancer

**[NCT04145700] Pediatric Cancer**
CAMPFIRE: A Study Evaluating Ramucirumab in Pediatric Patients and Young Adults With Relapsed, Recurrent, or Refractory Synovial Sarcoma

Pipeline information is current through April 28, 2022.
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