ERK1/2 Inhibitor

LY3214996
LY3214996 is a small molecule that has been shown in vitro to be a selective inhibitor of ERK1/2. ERK1/2 downstream cytoplasmic and nuclear targets involved in cell cycle, cell proliferation, cell growth, and cell survival. ERK1/2, also known as MAPK3 (ERK1) and MAPK1 (ERK2), are serine threonine kinases that serve as critical downstream targets of the MAPK pathway. Abnormalities of the MAPK pathway are common in many cancers, including cutaneous melanoma, uveal melanoma, colorectal cancer, non-small cell lung cancer, pancreatic ductal adenocarcinoma, and many others.

The mitogen-activated protein kinase (MAPK) pathway is a key regulator of cellular proliferation and 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**
- Advanced or metastatic cancer with an activating mitogen-activated protein kinase pathway alteration (dose expansion)
- Advanced or metastatic cancer (solid tumors) and would be an appropriate candidate for experimental therapy
- Metastatic BRAF V600E colorectal cancer
- Metastatic pancreatic ductal adenocarcinoma
- Advanced, unresectable cancer (dose escalation); advanced, unresectable cancer where otherwise stated in the inclusion criteria, of all clinically appropriate candidate for experimental therapy
- Mean QTc interval of ≤470 ms on screening electrocardiogram as calculated using the Bazett’s formula at several consecutive days of assessment
- Symptomatic central nervous system malignancy or metastasis
- Known HIV infection or activated/reactivated hepatitis A, B, or C
- Serious concomitant preexisting medical conditions
- Pregnant, breastfeeding, or planning to become pregnant
- History or findings of central or branch retinal artery or venous occlusion
- Current hematologic malignancies, acute or chronic leukemia
- Symptomatic central nervous system malignancy or metastasis
- Prior treatment within 28 days of the initial dose of study drug with an investigational product or any other type of medical research (clinical or nonclinical) that is likely to affect the absorption, distribution, metabolism, or elimination of LY3214996
- Symptomatic peripheral sensory neuropathy
- Second primary malignancy that may affect the interpretation of results
- Adequate organ function
- Discontinued previous treatments for cancer and resolution, except

**Key Exclusion Criteria**
- Ongo...