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产品名称：Acalisib
产品别名：GS-9820; CAL-120

生物活性：

Description

Acalisib is a potent and selective PI3Kδ inhibitor with an IC50 of 12.7 nM.

IC_{50} & Target

p110δ	p110γ	p110β	p110α	hVps34
12.7 nM (IC_{50})	1389 nM (IC_{50})	3377 nM (IC_{50})	5441 nM (IC_{50})	12682 nM (IC_{50})
DNA-PK				
18749 nM (IC_{50})				

In Vitro

Acalisib (GS-9820) is more selective for PI3Kδ (IC_{50}=12.7 nM) relative to other PI3K class I enzymes (IC_{50}: PI3Kα, 5,441 nM; PI3Kβ, 3,377 nM; PI3Kγ, 1,389 nM). Acalisib is also 10^3-fold more selective against PI3Kδ than against related kinases, such as PI3KCIIβ (IC_{50}>10 nM), hVPS34 (IC_{50}=12.7 μM), DNA-PK (IC_{50}=18.7 μM), and mTOR (IC_{50}>10 nM). In fibroblasts, the PDGF receptor signals through PI3Kα and the GPCR for lysophosphatidic acid (LPA) signals through PI3Kβ. Acalisib reduces PDGF-induced pAkt by only 50% at 11,585 nM, and LPA-induced pAkt by 50% at 2,069 nM.

In Vivo

To dissect the relative contribution of PI3Kα and PI3Kδ inhibition in the reduction of obesity, obese hyperphagic ob/ob mice are treated with a selective PI3Kα inhibitor, BYL-719, or with a selective PI3Kδ inhibitor, Acalisib (GS-9820). Remarkably, BYL-719 reduces body weight after 15 days of treatment to a similar extent as CNIO-PI3Ki, whereas Acalisib has no significant effect at the same doses as BYL-719. It should be noted that 10 mg/kg of Acalisib is sufficient to reduce the growth of multiple myeloma xenografts in mice[2].

Solvent&Solubility

In Vitro:

DMSO : 125 mg/mL (311.41 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4913 mL	12.4564 mL	24.9128 mL
	5 mM	0.4983 mL	2.4913 mL	4.9826 mL
	10 mM	0.2491 mL	1.2456 mL	2.4913 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month (protect from light)。 -80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (6.23 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (6.23 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.23 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.23 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.23 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.23 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Shugg RP, et al. Effects of isoform-selective phosphatidylinositol 3-kinase inhibitors on osteoclasts: actions on cytoskeletal organization, survival, and resorption. J Biol Chem. 2013 Dec 6;288(49):35346-57. [2]. Lopez-Guadamillas E, et al. PI3Kα inhibition reduces obesity in mice. Aging (Albany NY). 2016 Nov 4;8(11):2747-2753.

实验参考：

Cell Assay	The effect of inhibitors on RAW264.7 cell survival is evaluated using the MTT assay. RAW264.7 cells are seeded in Falcon flat bottom 96-well plates at a density of 2.5-3×10^4 cells/cm^2 in 100 μL of DMEM with 10% FBS and 1% antibiotic solution. After seeding, the cells are allowed to attach for 24 h then exposed to control or Acalisib (GS-9820) (100 pM to 10 μM) for 24 h. After incubation at 37°C in 5% CO_2, MTT substrate is added at a final concentration of 0.5 mg/mL for 4 h. Following a 4-h incubation, 100 μL of solubilization solution is added to each well to dissolve the formazan crystals and samples are analyzed after 24 h. Absorbance of the samples is assessed using a plate reader using a wavelength of 550 nm and a reference wavelength of 700 nm[1].
Animal Administration	Mice[2] Ob/ob C57BL6J mice and Wild-type C57BL6J/Ola.Hsd mice are housed under specific pathogen free (SPF) conditions, at 22°C, and with 12 hours dark/light cycles (light cycle from 8 am to 8 pm). All mice used are males of 20 weeks of age. Mice are fed with standard chow diet (18% of fat-based caloric content). PI3K inhibitors are administered daily by oral gavage during 15 or 16 days as follows, BYL-719 (5 and 10 mg/kg) and Acalisib (5 and 10 mg/kg), CNIO-PI3Ki (1 and 5 mg/kg), dissolved in PEG-300 and 10% N-methyl-2-pyrrolidone.
Kinase Assay	Biochemical in vitro lipid kinase assays are performed. A stock solution of Acalisib (GS-9820) is prepared in DMSO at a concentration of 10 mM. Ten-point kinase inhibitory activities are measured over a concentration range (5 to 10^4nM) with ATP at a concentration consistent with the K_m of each of the enzymes[1].
	[1]. Shugg RP, et al. Effects of isoform-selective phosphatidylinositol 3-kinase inhibitors on

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