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产品名称：GNE-477
产品别名：GNE-477

生物活性：

Description	GNE-477 is a potent and efficacious dual PI3K (IC50=4 nM)/mTOR(Ki=21 nM) inhibitor.	
IC_{50} & Target	PI3Kα	mTOR
	4 nM (IC_{50})	21 nM (Ki)
In Vitro	GNE-477 (Compound 8) has improved potency in the MCF7.1 cell proliferation assay with an EC50 of 143 nM[1].	
In Vivo	GNE-477 also exhibits stasis in a PC3 tumor growth inhibition study. In an experiment evaluating the tumor growth inhibition of a PC3 tumor xenograft over 14 days, stasis is achieved at a 20 mg/kg QD dose and significant inhibition is observed with doses as low as 1 mg/kg QD. GNE-477 is generally well tolerated during this study as demonstrated by acceptable levels of weight loss comparable to that observed with the animals in the vehicle cohort[1].	

Solvent&Solubility

In Vitro:

DMSO : 16.67 mg/mL (33.03 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9816 mL	9.9082 mL	19.8165 mL
	5 mM	0.3963 mL	1.9816 mL	3.9633 mL
	10 mM	0.1982 mL	0.9908 mL	1.9816 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。-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: ≥ 1.67 mg/mL (3.31 mM); Clear solution

此方案可获得 ≥ 1.67 mg/mL (3.31 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 16.699999 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: ≥ 1.67 mg/mL (3.31 mM); Clear solution

此方案可获得 ≥ 1.67 mg/mL (3.31 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 16.699999 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。
References	[1]. Heffron TP, et al. Identification of GNE-477, a potent and efficacious dual PI3K/mTOR inhibitor. Bioorg Med Chem Lett. 2010 Apr 15;20(8):2408-11.

实验参考：

Animal Administration	Mice, Rats and Dogs[1] Female nu/nu mice are dosed with the GNE-477 HCl salt as a solution intraveinously (1 mg/kg) in 5% DMSO/5% cremophor and dosed orally as a solution in 80% PEG (5 mg/kg). Male rats are dosed with the GNE-477 TFA salt as a solution intraveinously (1 mg/kg) in 5% DMSO/5% cremophor and dosed orally as a solution in 80% PEG (5 mg/kg). Male beagle dogs are dosed with the GNE-477 HCl salt as a solution intraveinously (1 mg/kg) in 10% HP-β-CD and dosed orally as a suspension in MCT (2 mg/kg). Efficacy study of GNE-477 in the PC3-NCI tumor xenograft model is proformed. The percent of tumor growth inhibition (TGI) at the end of study (day 14) is measured and compared with the vehicle control group.
References	[1]. Heffron TP, et al. Identification of GNE-477, a potent and efficacious dual PI3K/mTOR inhibitor. Bioorg Med Chem Lett. 2010 Apr 15;20(8):2408-11.