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产品名称：GNE-495
产品别名：GNE-495

生物活性：

Description	GNE-495 is a potent and selective MAP4K4 inhibitor with an IC_{50} of 3.7 nM.
IC_{50} & Target	MAP4K4
	3.7 nM (IC_{50})
In Vitro	GNE-495 is a potent and selective MAP4K4 inhibitor with efficacy in retinal angiogenesis. GNE-495 shows the best balance of MAP4K4 inhibition, permeability, microsomal stability, and cellular potency[1].
In Vivo	GNE-495 is administered intraperitoneally to neonatal mouse pups at high doses: 25 and 50 mg/kg. GNE-495 shows good in vivo profile in all species tested, with low clearances, moderate terminal half-lives, and reasonable oral exposure levels (F=37-47%)[1].

Solvent&Solubility

In Vitro:

DMSO : 2.17 mg/mL (5.35 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4666 mL	12.3329 mL	24.6658 mL
	5 mM	0.4933 mL	2.4666 mL	4.9332 mL
	10 mM	---	---	---

*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: ≥ 0.22 mg/mL (0.54 mM); Clear solution

此方案可获得 ≥ 0.22 mg/mL (0.54 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 2.2 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: ≥ 0.22 mg/mL (0.54 mM); Clear solution

此方案可获得 ≥ 0.22 mg/mL (0.54 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 2.2 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: ≥ 0.22 mg/mL (0.54 mM); Clear solution 此方案可获得 ≥ 0.22 mg/mL (0.54 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 2.2 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Ndubaku CO et al. Structure-Based Design of GNE-495, a Potent and Selective MAP4K4 Inhibitor with Efficacy in Retinal Angiogenesis. ACS Med Chem Lett. 2015 Jun 29;6(8):913-8.

实验参考：

Animal Administration	Rats, Mice and Pups [1] For the brain cassette study, three male Sprague-Dawley (SD) rats are dosed with intravenous (IV) bolus of six test compounds (e.g., GNE-495; 0.5 mg/kg). For the mouse PK study, female CD-1 mice are administered IV bolus doses of GNE-495 (1 mg/kg). In addition, female CD-1 mice are administered GNE-495 (5 mg/kg) via oral (PO) gavage. A dosing volume of 2 mL/kg is used for the rat brain cassette PK and 5 mL/kg is used for all other dosing. Animals are not fasted prior to dose administration, and water and food are available ad libitum. Following administration of the compound of interest, three blood samples (~60 μL) are collected at each time point from individual mice up to either 9 or 24 hours post-dose using a serial sampling approach. Immediately upon collection, the blood is mixed with K2EDTA and stored on ice or in a chilled Kryorack prior to centrifugation to obtain plasma. Within 1 hr of collection, blood samples are centrifuged at approximately 1000-2000× g for 10-15 min at 4°C, and plasma is harvested. The plasma samples are stored at -70 to -80°C until analysis. For neonate PK, 3-day old CD1 pups are injected with 25 mg/kg and 50 mg/kg GNE-495 intraperitoneally, blood samples are collected at the time points indicated, retinas are collected one hour post-dose and snap frozen in liquid nitrogen and stored at -80°C until analysis. Plasma and retinal lysate concentrations are determined by LC/MS/MS.
References	[1]. Ndubaku CO et al. Structure-Based Design of GNE-495, a Potent and Selective MAP4K4 Inhibitor with Efficacy in Retinal Angiogenesis. ACS Med Chem Lett. 2015 Jun 29;6(8):913-8.