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产品名称：ROR gamma-t-IN-1
产品别名：GSK805

生物活性：

Description

GSK805 is a potent, orally bioavailable, and CNS penetrant **RORγt** inhibitor with pIC_{50} of 8.4 and >8.2 for RORγ FRET assay and Th17 assay[1].

IC_{50} & Target

IC50: 8.4 (RORγt)[1]

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (187.84 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8784 mL	9.3921 mL	18.7843 mL
	5 mM	0.3757 mL	1.8784 mL	3.7569 mL
	10 mM	0.1878 mL	0.9392 mL	1.8784 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: ≥ 2.5 mg/mL (4.70 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.70 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% corn oil

Solubility: ≥ 2.5 mg/mL (4.70 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.70 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]. Wang Y, et al. Discovery of Biaryl Amides as Potent, Orally Bioavailable, and CNS Penetrant RORγt Inhibitors. ACS Med Chem Lett. 2015 May 26;6(7):787-792.

实验参考：

Animal Administration	Animal administration[1] GSK805 are orally administered once daily at 3 doses (1, 3, and 10 mg/kg) to EAE mice from the day of immunization. Compared to the control, the treatment with 9a or 9g resulted in a delay and significant reduction in clinical severity of EAE in a dose-dependent manner. Compared to thiazole ketone amide 2, which only showed EAE efficacy up to day 20 at 100 mg/kg twice daily dosing,32 the biaryl amides 9a and 9g are much more efficacious. This could be attributed to their good in vitro activities as well as much improved oral exposure and CNS penetration. However, it should be noted that although 9g had more brain exposure than 9a, it exhibited less efficacy than 9a in EAE experiments, indicating that there might be additional factors such as "free" brain concentration affecting in vivo efficacy[1].
References	[1]. Wang Y, et al. Discovery of Biaryl Amides as Potent, Orally Bioavailable, and CNS Penetrant RORγt Inhibitors. ACS Med Chem Lett. 2015 May 26;6(7):787-792.