产品名称：GSK2269557 (free base)
产品别名：Nemiralisib

生物活性：

Description	Nemiralisib (GSK2269557 free base) is a potent and highly selective **PI3Kδ** inhibitor with a **pK**$_i$ of 9.9.

IC_{50} & Target	PI3Kδ	PI3Kγ	PI3Kα	PI3Kβ
	9.9 (pKi)	5.2 (pIC_{50})	5.3 (pIC_{50})	5.8 (pIC_{50})

In Vitro	Nemiralisib (GSK2269557 free base) is highly selective for PI3Kδ, with >1000-fold selectivity over the closely related isoforms PI3Kα (pIC50=5.3), PI3Kβ (pIC50=5.8) and PI3Kγ (pIC50=5.2). Nemiralisib inhibits IFNγ in the peripheral blood mononuclear (PBMC) assay with an pIC50 of 9.7[1].
In Vivo	To assess the suitability of the series for inhaled delivery clearance data in rat microsomes and subsequently in vivo pharmacokinetic data from Sprague Dawley male rats is obtained. Compounds (e.g., Nemiralisib) are administered by the oral or intravenous routes, at a dose level of 3 and 1mg/kg respectively (n=2 rats/route). Nemiralisib free base is active in a disease relevant brown norway rat acute OVA model of Type 2 helper T-cells (Th2)-driven lung inflammation[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 31 mg/mL (70.37 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2699 mL	11.3497 mL	22.6994 mL
	5 mM	0.4540 mL	2.2699 mL	4.5399 mL
	10 mM	0.2270 mL	1.1350 mL	2.2699 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。

References

[1]. Down K et al. Optimization of Novel Indazoles as Highly Potent and Selective Inhibitors of Phosphoinositide 3-Kinase δ for the Treatment of Respiratory Disease. J Med Chem. 2015 Sep 24;58(18):7381-99.

实验参考：

Animal Administration	Rats[1] In vivo pharmacokinetics is tested in Sprague Dawley male rats. Compounds (e.g., Nemiralisib) are administered discretely by the oral or intravenous routes, at a dose level of 3 and 1 mg/kg respectively (n=2 rats/route). Compounds (e.g., Nemiralisib) are formulated as a solution in DMSO:PEG200:water (5:45:50 v/v/v) at a dose volume of 6 (oral) and 2 (intravenous) mL/kg. All animals are serially bled from the tail vein and blood samples collected over a time-course of 0-7 h are submitted to LC-MS/MS analysis for the quantification of the parent compound. The main pharmacokinetic parameters are estimated by non-compartmental analysis.
References	[1]. Down K et al. Optimization of Novel Indazoles as Highly Potent and Selective Inhibitors of Phosphoinositide 3-Kinase δ for the Treatment of Respiratory Disease. J Med Chem. 2015 Sep 24;58(18):7381-99.

源叶生物