产品名称：
3-(9-fluoro-2-(piperidine-1-carbonyl)-1,2,3,4-tetrahydro-[1,4]diazepino[6,7,1-hi]indol-7-yl)-4-(imidazo[1,2-a]pyridin-3-yl)-1H-p
产品别名：**LY2090314**

生物活性：

Description	LY2090314 is a potent inhibitor of glycogen synthase kinase-3 (GSK-3) with IC_{50} values of 1.5 nM and 0.9 nM for GSK-3α and GSK-3β, respectively.	
IC_{50} & Target [1]	GSK-3β	GSK-3α
	0.9 nM (IC_{50})	1.5 nM (IC_{50})
In Vitro	LY2090314 (20 nM) promotes a time-dependent stabilization of β-catenin total protein as well as an induction of Axin2. LY2090314 is highly selective towards GSK3 as demonstrated by its fold selectivity relative to a large panel of kinases. LY2090314 potently induces apoptotic cell death in a panel of melanoma cell lines irrespective of BRAF mutation status. Cell death induced by LY2090314 is dependent on β-catenin and GSK3β knockdown increases the sensitivity of cells to LY2090314. LY2090314 remains active in cell lines resistant to PLX4032 and has an independent mechanism of action[2].	
In Vivo	LY2090314 exhibits high clearance (approximating hepatic blood flow) and a moderate volume of distribution (appr 1-2 L/kg) resulting in rapid elimination (half-life appr 0.4, 0.7, and 1.8-3.4 hours in rats, dogs, and humans, respectively). LY2090314 is rapidly cleared by extensive metabolism with negligible circulating metabolite exposures due to biliary excretion of metabolites into feces with no apparent intestinal reabsorption[1]. LY2090314 (25 mg/kg Q3D, i.v.) elevates Axin2 gene expression in vivo, demonstrates single agent activity in the A375 xenograft model of melanoma and enhances the efficacy of DTIC[2].	

Solvent&Solubility

In Vitro:

DMSO : ≥ 31 mg/mL (60.48 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9511 mL	9.7555 mL	19.5111 mL
	5 mM	0.3902 mL	1.9511 mL	3.9022 mL
	10 mM	0.1951 mL	0.9756 mL	1.9511 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 (4.88 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.88 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。
References	[1]. Zamek-Gliszczynski MJ, et al. Pharmacokinetics, metabolism, and excretion of the glycogen synthase kinase-3 inhibitor LY2090314 in rats, dogs, and humans: a case study in rapid clearance by extensive metabolism with low circulating metabolite exposure. Dr [2]. Atkinson JM, et al. Activating the Wnt/β-Catenin Pathway for the Treatment of Melanoma--Application of LY2090314, a Novel Selective Inhibitor of Glycogen Synthase Kinase-3. PLoS One. 2015 Apr 27;10(4):e0125028.

实验参考：

Animal Administration	Five million A375 human melanoma cancer cells are injected S.C. in the flank of female 6 to 8 week old athymic nude mice in a 1:1 mixture with matrigel. Mice are monitored daily for palpable tumors. When tumors reach appr 100 mm^2 mice are randomized into groups receiving either LY2090314 (25 mg/kg Q3D) or vehicle (20% Captisol/0.01N HCl) via i.v. administration. Tumor volume (measured by calipers) and animal body weight are recorded twice weekly. Tumor volumes are calculated using the formula: $(a^2 \times b)/2$ (a being the smaller and b being the larger dimension of the tumor). For combination studies with DTIC (60 mg/kg QD), LY2090314 is dosed at 2.5 mg/kg Q3D and tumor growth monitored. [2]
References	[1]. Zamek-Gliszczynski MJ, et al. Pharmacokinetics, metabolism, and excretion of the glycogen synthase kinase-3 inhibitor LY2090314 in rats, dogs, and humans: a case study in rapid clearance by extensive metabolism with low circulating metabolite exposure. Dr [2]. Atkinson JM, et al. Activating the Wnt/β-Catenin Pathway for the Treatment of Melanoma--Application of LY2090314, a Novel Selective Inhibitor of Glycogen Synthase Kinase-3. PLoS One. 2015 Apr 27;10(4):e0125028.