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产品名称：RIP2 kinase inhibitor 1
产品别名：GSK2983559 active metabolite

生物活性：

Description	GSK2983559 active metabolite is an active metabolite of GSK2983559. GSK2983559 active metabolite is a receptor interacting protein-2 (RIP2) kinase inhibitor extracted from patent WO/2014043446 A1, compound example 1.
IC_{50} & Target	RIP2 Kinase[1]
In Vitro	GSK2983559 active metabolite is a novel prodrug of a quinazolyl amine that inhibits RIP2 kinase. Receptor interacting protein-2 (RIP2) kinase, which is also referred to as CARD3, RICK, CARDIAK, or RIPK2, is a TKL family serine/threonine protein kinase involved in innate immune signaling. RIP2 kinase is composed of an N-terminal kinase domain and a C-terminal caspase-recruitment domain (CARD) linked via an intermediate (IM) region. The CARD domain of RIP2 kinase mediates interaction with other CARD-containing proteins, such as NODI and NOD2. NODI and NOD2 are cytoplasmic receptors which play a key role in innate immune surveillance. They recognize both gram positive and gram negative bacterial pathogens and are activated by specific peptidoglycan motifs, diaminopimelic acid (i.e., DAP) and muramyl dipeptide[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 25 mg/mL (54.52 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1808 mL	10.9039 mL	21.8079 mL
	5 mM	0.4362 mL	2.1808 mL	4.3616 mL
	10 mM	0.2181 mL	1.0904 mL	2.1808 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 (5.45 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.45 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

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 (5.45 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.45 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]. Linda N. Casillas, et al. Prodrugs of amino quinazoline kinase inhibitor. PCT Int. Appl. (2014), WO 2014043446 A1 20140320.

实验参考：

Animal Administration	Rats[1] Rats are orally pre-dosed with RIP2 kinase inhibitor 1, at a dose of 2 mg/kg (8 rats) and with Prednisolone (8 rats, used as a positive control), followed by dosing with L18-MDP (50 μg/rat) 0.25 h/min after pre-dosing. Combined cytokine levels (IL8, TNFa, IL6 and IL-Iβ) in whole blood samples taken from the rats in this study are measured using an antibody based detection. The combined cytokine response is calculated as the averaged response for the 4 cytokines measured relative to the response observed in the vehicle-treated mice, and are depicted as the mean±standard error of the mean (n=8 rats/group).
References	[1]. Linda N. Casillas, et al. Prodrugs of amino quinazoline kinase inhibitor. PCT Int. Appl. (2014), WO 2014043446 A1 20140320.