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产品名称：Talmapimod
产品别名：他匹莫德 ；SCIO-469

生物活性：

Description	Talmapimod (SCIO-469) is an orally active, selective, and ATP-competitive p38α inhibitor with IC_{50} of 9 nM, shows about 10-fold selectivity over p38β, and at least 2000-fold selectivity over a panel of 20 other kinases, including other MAPKs.
IC_{50} & Target	IC50: 9 nM (p38)[1].
In Vitro	Talmapimod (SCIO-469) decreases constitutive p38α MAPK phosphorylation of both 5T2MM and 5T33MM cells. Talmapimod (SCIO-469) also inhibits secretion and expression of the osteoclast-activating factors IL-11, receptor activator of NF-κB ligand, and macrophage inflammatory protein 1α, and prevents human osteoclast activationIn. It can also inhibit multiple myeloma growth and prevents bone disease in the 5T2MM and 5T33MM models[2]. Talmapimod (SCIO-469) inhibits LPS-induced TNF-a production in human whole blood[3].
In Vivo	Targeting p38α MAPK with Talmapimod (SCIO-469) decreases myeloma burden in addition to preventing the development of myeloma bone disease[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (194.93 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9493 mL	9.7466 mL	19.4932 mL
	5 mM	0.3899 mL	1.9493 mL	3.8986 mL
	10 mM	0.1949 mL	0.9747 mL	1.9493 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 (4.87 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (4.87 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% (20% SBE-β-CD in saline)

	Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.87 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 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: ≥ 2.5 mg/mL (4.87 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.87 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]. Hideshima T et al. p38 MAPK inhibition enhances PS-341 (bortezomib)-induced cytotoxicity against multiple myeloma cells. Oncogene. 2004 Nov 18, 23(54), 8766-76. [2]. Navas T, et al. Inhibition of p38alpha MAPK disrupts the pathological loop of proinflammatory factor production in the myelodysplastic syndrome bone marrow microenvironment. Leuk Lymphoma. 2008 Oct;49(10):1963-75. [3]. Vanderkerken K et al. Inhibition of p38alpha mitogen-activated protein kinase prevents the development of osteolytic bone disease,reduces tumor burden, and increases survival in murine models of multiple myeloma. Vanderkerken K et al.

实验参考：

Cell Assay	5TMM cells (0.5 × 106/mL) were pretreated with different concentrations of Talmapimod (SCIO-469) in serum-free medium and then placed in the lower compartment of a Transwell system. Syngeneic bone marrow stromal cells were seeded into the Transwell itself. After 18 h, the 5TMM cells were collected from the lower compartment and stained for active caspase-3 with a FITC-labeled antibody according to manufacturer's instructions
Animal Administration	Animal injection[1] For studies of the effect of Talmapimod (SCIO-469) on myeloma development, three groups of male mice (n = 12) were injected i.v. with 0.5 × 106 5T33MM cells. Mice were left untreated (naive) or, if injected with tumor cells, treated from the time of tumor cells injection with either Talmapimod (SCIO-469) (150 or 450 mg/kg powder diet continuously available for the mice) or a vehicle (PBS) until the first mice showed signs of morbidity (at 3.7 weeks).
References	[1]. Hideshima T et al. p38 MAPK inhibition enhances PS-341 (bortezomib)-induced cytotoxicity against multiple myeloma cells. Oncogene. 2004 Nov 18, 23(54), 8766-76. [2]. Navas T, et al. Inhibition of p38alpha MAPK disrupts the pathological loop of proinflammatory factor production in the myelodysplastic syndrome bone marrow microenvironment. Leuk Lymphoma. 2008 Oct;49(10):1963-75. [3]. Vanderkerken K et al. Inhibition of p38alpha mitogen-activated protein kinase prevents the development of osteolytic bone disease,reduces tumor burden, and increases survival in murine models of multiple myeloma. Vanderkerken K et al.