Talmapimod

Cat. No.: HY-10406

CAS No.: 309913-83-5

Molecular Formula: $C_{27}H_{30}ClFN_4O_3$

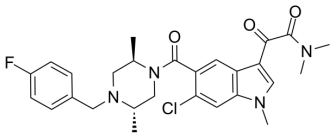
Molecular Weight: 513

Target: p38 MAPK

Pathway: MAPK/ERK Pathway

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (194.93 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / 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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (4.87 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Talmapimod (SCIO-469) is an orally active, selective, and ATP-competitive p38α inhibitor with an IC_{50} of 9 nM. Talmapimod shows about 10-fold selectivity over p38β, and at least 2000-fold selectivity over a panel of 20 other kinases, including other MAPKs[1][2][3].

IC_{50} & Target	p38α	p38β
	9 nM (IC_{50})	90 nM (IC_{50})

In Vitro

Talmapimod (SCIO-469) (100-200 nM; 1 hour) inhibits phosphorylation of p38 MAPK in MM cells[1].
Talmapimod inhibits LPS-induced TNF-a production in human whole blood[2].
Talmapimod decreases constitutive p38alpha MAPK phosphorylation of both 5T2MM and 5T33MM cells[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	MM.1S, U266, RPMI8226, MM.1R, and RPMI-Dox40 cell lines
Concentration:	100, 200 nM
Incubation Time:	1 hour
Result:	Strongly inhibits phosphorylation of p38 MAPK.

In Vivo

Targeting p38α MAPK with Talmapimod (SCIO-469) decreases myeloma burden in addition to preventing the development of myeloma bone disease[2].
Talmapimod inhibits multiple myeloma growth and prevents bone disease in the 5T2MM and 5T33MM models[3].
Talmapimod (10-90 mg/kg; p.o.; twice daily orally for 14 days) dose-dependently reduced tumor growth and also dose-dependently reduced weight of the palpable tumors at termination[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Six-week-old male triple immune-deficient BNX mice (RPMI-8226 MM palpable tumors)[4]
Dosage:	P.o.; twice daily orally for 14 days
Administration:	10, 30, 90 mg/kg
Result:	Dose-dependently reduced tumor growth.

CUSTOMER VALIDATION

- Cell. 2020 Aug 6;182(3):685-712.e19.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Biol Toxicol. 2021 Aug;37(4):515-529.

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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]. 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. Cancer Res. 2007 May 15;67(10):4572-7.

[3]. 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.

[4]. Medicherla S, et al. p38alpha-selective MAP kinase inhibitor reduces tumor growth in mouse xenograft models of multiple myeloma. Anticancer Res. 2008 Nov-Dec;28(6A):3827-33.

Caution: Product has not been fully validated for medical applications. For research use only.

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