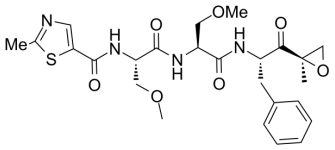
Oprozomib

Cat. No.:	HY-12113
CAS No.:	935888-69-0
Molecular Formula:	$C_{25}H_{32}N_4O_7S$
Molecular Weight:	532.61
Target:	Proteasome; Autophagy
Pathway:	Metabolic Enzyme/Protease; Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (93.88 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8775 mL	9.3877 mL	18.7755 mL
5 mM	0.3755 mL	1.8775 mL	3.7551 mL
10 mM	0.1878 mL	0.9388 mL	1.8775 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: ≥ 2.08 mg/mL (3.91 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.91 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Oprozomib (PR-047) is an orally bioavailable and selective peptide epoxyketone proteasome inhibitor with IC_{50}s of 36 and 82 nM for proteasome (β5) and immunoproteasome (LMP7), respectively. Oprozomib (ONX 0912) induces apoptosis in MM cells[1].

In Vitro

Oprozomib inhibits 20S chymotrypsin-like (CT-L) with an IC_{50} of 55 ± 19 nM. Oprozomib inhibits human leukemia Molt-4 cells CT-L with an IC_{50} of 66 nM[1].

Oprozomib (ONX 0912; 1-1000 nM; 48 hours) significantly decreases the viability of human multiple myeloma (MM) cell lines [2].

The anti-MM activity of Oprozomib is associated with activation of caspase-8, caspase-9, caspase-3, and PARP[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	Human MM cell lines (MM.1S, INA-6, RPMI-8226, MM.1R, Dox-40, KMS12, and OPM2)
Concentration:	1, 10, 100, 1000 nM
Incubation Time:	48 hours
Result:	Exhibited anti-MM activity.

Western Blot Analysis[2]

Cell Line:	MM.1S cells
Concentration:	7 nM and 10 nM
Incubation Time:	48 hours
Result:	Treatment with 3nM triggered a marked increase in proteolytic cleavage of PARP, a signature event during apoptosis. Induced cleavage of caspase-3, an upstream activator of PARP.Induced activation of both casapse-8 (extrinsic) and caspase-9 (intrinsic) apoptotic pathways.

In Vivo

Oprozomib (PR-047) selectively inhibits chymotrypsin-like (CT-L) activity of both the constitutive proteasome (β5) and immunoproteasome (LMP7) and demonstrates an absolute bioavailability of up to 39% in rodents and dogs[1].

Oprozomib promotes antitumor activity in multiple animal models by oral administration at doses below the maximum tolerated dose (MTD)[1].

Oprozomib (30 mg/kg by oral gavage once daily for 5 consecutive days followed by 2 days of rest) treatment decreases tumor burden in C57Bl/6 and NOD.SCID.IL2Rγ$^{-/-}$ mice[3].

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Animal Model:	C57Bl/6 and NOD.SCID.IL2Rγ$^{-/-}$ mice bearing established human RPMI-8226-luc myeloma cells[3]
Dosage:	30 mg/kg
Administration:	Oral gavage once daily for 5 consecutive days followed by 2 days of rest
Result:	Decreased human MM tumor burden and protects mice from bone destruction.

REFERENCES

[1]. Han-Jie Zhou, et al. Design and synthesis of an orally bioavailable and selective peptide epoxyketone proteasome inhibitor (PR-047). J Med Chem. 2009 May 14;52(9):3028-38.

[2]. Dharminder Chauhan,et al. A novel orally active proteasome inhibitor ONX 0912 triggers in vitro and in vivo cytotoxicity in multiple myeloma. Blood. 2010 Dec 2;116(23):4906-15.

[3]. M A Hurchla, et al.The epoxyketone-based proteasome inhibitors carfilzomib and orally bioavailable oprozomib have anti-resorptive and bone-anabolic activity in addition to anti-myeloma effects. Leukemia. 2013 Feb;27(2):430-40.

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

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