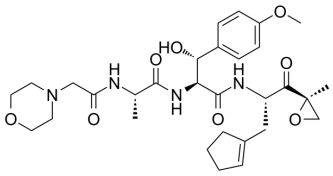
Zetomipzomib

Cat. No.:	HY-114419
CAS No.:	1629677-75-3
Molecular Formula:	$C_{30}H_{42}N_4O_8$
Molecular Weight:	586.68
Target:	Proteasome
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Zetomipzomib (KZR-616), a first-in-class inhibitor of the immunoproteasome, selectively targets the LMP7 (IC_{50}: 39/57 nM=hLMP7/mLMP7) and LMP2 (IC_{50}: 131/179 nM=hLMP7/mLMP7) subunits of the immunoproteasome. Zetomipzomib has the potential for the research of multiple autoimmune diseases[1][2].

In Vitro

Zetomipzomib also inhibits MECL-1 subunit (IC_{50}=623 nM) and constitutive proteasome β5 subunit (IC_{50}=688 nM). Zetomipzomib maintains LMP7 and LMP2 selective inhibition in MOLT-4 cells. Zetomipzomib (250 nM) shows a comparable cytokine inhibition profile peripheral blood mononuclear cells (PBMC)[1].Zetomipzomib is an immunoproteasome-selective inhibitor identified based on the optimization of ONX-0914 (HY-13207) and PR-924 (HY-123587)[3].

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

In Vivo

Zetomipzomib (5 mg/kg; i.v.; dosing was repeated on days 6, 8, 11, and 13) shows efficacy in the anticollagen antibody induced arthritis (CAIA) model[1].

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

Animal Model:	7-8 week old female BALB/c mice (CAIA model)[1]
Dosage:	I.v.; Dosing was repeated on days 6, 8, 11, and 13 until for 15 day
Administration:	5 mg/kg
Result:	Showed efficacy in the anticollagen antibody induced arthritis (CAIA) model.

REFERENCES

[1]. Johnson HWB, et al. Required Immunoproteasome Subunit Inhibition Profile for Anti-Inflammatory Efficacy and Clinical Candidate KZR-616 ((2 S,3 R)- N-((S)-3-(Cyclopent-1-en-1-yl)-1-((R)-2-methyloxiran-2-yl)-1-oxopropan-2-yl)-3-hydroxy-3-(4-methoxyphenyl)-2-((S)-2-(2-morpholinoacetamido)propanamido)propenamide). J Med Chem. 2018 Dec 27;61(24):11127-11143.

[2]. Muchamuel T, et al. FRI0296 Kzr-616, a selective inhibitor of the immunoproteasome, blocks the disease progression in multiple models of systemic lupus erythematosus (SLE). Annals of the Rheumatic Diseases 2018;77:685.

[3]. Xi J, et al. Immunoproteasome-selective inhibitors: An overview of recent developments as potential drugs for hematologic malignancies and autoimmune diseases.

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