DN-1289

Cat. No.: HY-152142

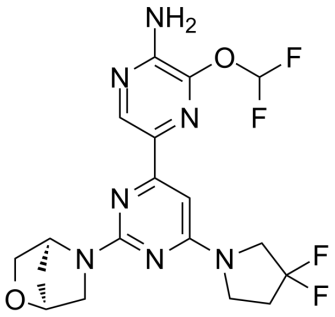
Molecular Formula: $C_{18}H_{19}F_4N_7O_2$

Molecular Weight: 441.38

Target: JNK

Pathway: MAPK/ERK Pathway

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

DN-1289 is an orally active and selective inhibitor of dual leucine zipper kinase (DLK; IC_{50}=17 nM) and leucine zipper-bearing kinase (LZK; IC_{50}=40 nM). DN-1289 results significant attenuation of optic nerve crush (ONC)-induced p-c-Jun in mice model. DN-1289 has excellent in vivo plasma half-life and blood-brain barrier permeability[1].

IC_{50} & Target

IC50: 17 nM (DLK), 40 nM (LZK)[1]

In Vitro

DN-1289 (compound 14) (0.1, 0.3, and 1 μM; 0-20 h) can block axon degeneration in dorsal root ganglion (DRG) neurons induced by nerve growth factor (NGF) withdrawal[1].

DN-1289 (0.1, 0.3, and 1 μM; 0-20 h) inhibits the activation of caspases in DRG neurons over time induced by NGF withdrawal [1].

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

In Vivo

DN-1289 (compound 14) (100 mg/kg and 150 mg/kg; i.p.; once daily for 10-15 d) is well-tolerated in mice model[1].

DN-1289 (150 mg/kg; p.o.; b.i.d. for 10 d) inhibits phosphorylation of c-Jun in an acute injury model with optic nerve crush (ONC) application[1].

Pharmacokinetic Analysis[1]

Species	Route	Dose (mg/kg)	plasma C_{max} (μM)	plasma $AUC_{0-24\ h}$ (μM·h)	CL_p (mL/min/kg)	CL_u (mL/min/kg)	V_d (L/kg)	$t_{1/2}$ (h)	F (%)	Kp_{uu} (AUC)	brain AUC $_{0-2\ h}$ (μM·h)
rat	IV	1	1.09	2.42	14.7	150	6.7	6.5	/	0.6	4.05
	PO	3	0.58	3.9	/	/	/	4.6	52	/	/
mouse	IV	1	1.06	4.06	8.6	200	4.7	6.8	/	/	/
	PO	10	2.32	21.9	/	/	/	7.9	56	0.4	6.91

	PO	150	24.9	324	/	/	/	23.7	53	/	/
	IP	100	15.4	280	/	/	/	23.7	53	/	/
cyno	IV	0.5	0.746	2.79	6.1	64	3.4	7.9	/	/	/

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

REFERENCES

[1]. Craig RA 2nd, et al. Discovery of Potent and Selective Dual Leucine Zipper Kinase/Leucine Zipper-Bearing Kinase Inhibitors with Neuroprotective Properties in In Vitro and In Vivo Models of Amyotrophic Lateral Sclerosis. J Med Chem. 2022 Dec 22;65(24):16290-16312.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA