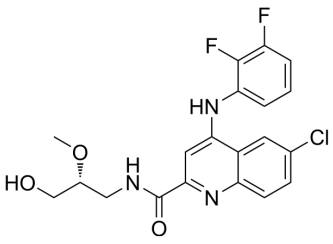
20S Proteasome-IN-4

Cat. No.:	HY-151195
CAS No.:	2827061-47-0
Molecular Formula:	$C_{20}H_{18}ClF_2N_3O_3$
Molecular Weight:	421.83
Target:	Proteasome; Parasite
Pathway:	Metabolic Enzyme/Protease; Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	20S Proteasome-IN-4 (Compound 7) is a brain-penetrant, parasite-selective, orally active 20S proteasome inhibitor with an IC_{50} of 6.3 nM against T. b. brucei 20S proteasome. 20S Proteasome-IN-4 can be used for the research of human African trypanosomiasis (HAT)[1].
IC_{50} & Target	IC_{50}: 6.3 nM (T. b. brucei 20S proteasome)[1]
In Vitro	20S Proteasome-IN-4 (Compound 7) (24 h) inhibits T. b. brucei growth with an EC_{50} of <2.5 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	20S Proteasome-IN-4 (Compound 7) (3 mg/kg; i.g.; once a day for 4 days) cures a stage I mouse model of human African trypanosomiasis[1]. 20S Proteasome-IN-4 (15 mg/kg; i.g.; twice a day for 1 week) cures a stage II mouse model of human African trypanosomiasis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	NMRI mice, hemolymphatic mice model (Stage I)[1]
Dosage:	3 mg/kg
Administration:	Oral gavage, once a day for 4 days
Result:	Achieved complete cure of the stage I infection.

Animal Model:	CD1 mice, meningoncephalic mice model (stage II)[1]
Dosage:	15 mg/kg
Administration:	Oral gavage, twice a day for 1 week
Result:	Achieved complete cure of the stage II infection.

Animal Model:	BALB/c mice and Wistar rats[1]

Dosage:	1 mg/kg or 3 mg/kg
Administration:	Intravenous or oral administration (Pharmacokinetic Analysis)
Result:	ADME and PK Data for 20S Proteasome-IN-4 (Compound 7)[1]

cmp	solubility pH 6.8 μM	LM CL_{int} (m/r) [μL/min/mg]	LM scaled CL_{int} [mL/min/kg] (m/r)	f_u plasma [%] (m/r)	CL_p [mL/min/kg] (m/r)	CL_u [mL/min/kg] (m/r)	AUC_{PO} [μM•h] (m/r)	AUC_{IV} [μM•h] (m/r)	%F m/r
20S Proteasome-IN-4	12	79/66	311/119	1.0/1.6	17/9	1700/563	5.2/17	2.3/4.4	76/128

Solubility: Miniaturized shake flask solubility in phosphate buffer; $f_{u,plasma}$ from PPB; LM scaled Cl_{int} = (LM Cl_{int}•SF1•SF2)/1000 with SF1 (mg protein per g liver) m,r = 45, SF2 (g liver per kg BW); m = 87.5, SF2 r = 40. Unbound clearance: $Cl_p = Cl_u/f_u$, with Cl_p observed clearance. Mouse and rat PK 1 mpk IV/3 mpk PO.

REFERENCES

[1]. Koester DC, et al. Discovery of Novel Quinoline-Based Proteasome Inhibitors for Human African Trypanosomiasis (HAT). J Med Chem. 2022 Aug 22.

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