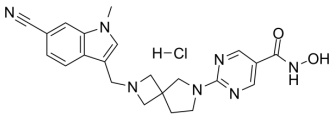
HDAC1-IN-3

Cat. No.:	HY-144297
CAS No.:	2482998-35-4
Molecular Formula:	$C_{22}H_{24}ClN_7O_2$
Molecular Weight:	453.92
Target:	HDAC; Parasite
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

HDAC1-IN-3 is a potent Pf HDAC1 inhibitor. HDAC1-IN-3 shows antimalarial activity in wild-type and multidrug-resistant parasite strains. HDAC1-IN-3 shows a significant in vivo killing effect against all life cycles of parasites[1].

IC_{50} & Target

HDAC1 2.2 nM (IC_{50})	HDAC2 5.1 nM (IC_{50})	HDAC3 5.2 nM (IC_{50})	HDAC6 85.5 nM (IC_{50})
HDAC8 29.9 nM (IC_{50})	Plasmodium		

In Vitro

HDAC1-IN-3 (compound JX35) shows antimalarial activity with IC_{50}s of 1.26 nM and 1.61 nM for wild-type Plasmodium falciparum (P. falciparum) parasite 3D7 and chloroquine-resistant P. falciparum parasite Dd2, respectively[1].

HDAC1-IN-3 (10 μM; 72 h) shows low cytotoxicity with IC_{50}s of 1.02 μM and 1.21 μM for HepG2, 293T cells, respectively[1].

HDAC1-IN-3 (72 h) shows no cross-resistance with clinical antimalarial drugs with IC_{50}s of 3.06, 2.18, 5.85 nM for GB4, C2A, CP286, respectively[1].

HDAC1-IN-3 (10, 30, 60, 100 nM; 3, 6, 12, 24 h) shows antimalarial activity in a time- and dose-dependent manner with asynchronous 3D7 parasites[1].

HDAC1-IN-3 (40 nM, 4 days; P. falciparum 3D7 cells) shows the killing effects of JX35 on P. falciparum parasites during asexual reproduction stages might be related to the inhibition of schizont growth and reinvasion of RBCs (red blood cells)[1].

HDAC1-IN-3 (5, 20 nM; 4 h) inhibits the expression of Pf HDAC against ART (artemisinin)-resistant parasite strains[1].

HDAC1-IN-3 reduces the inhibition of hHDACs with IC_{50}s of 2.2, 5.1, 5.2, 85.5, 29.9 nM for HDAC1, HDAC2, HDAC3, HDAC6, HDAC8, respectively[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	HepG2, 293T cells
Concentration:	10 μM
Incubation Time:	72 h
Result:	Showed low cytotoxicity with IC_{50}s of 1.02 μM and 1.21 μM for HepG2, 293T cells, respectively.

Western Blot Analysis[1]

Cell Line:	P. falciparum 3D7 cells
Concentration:	5, 20 nM
Incubation Time:	4 h
Result:	Inhibited the expression of Pf HDAC against ART (artemisinin)-resistant parasite strains.

In Vivo

HDAC1-IN-3 (30, 60, 90 mg/kg; i.p.; once daily for 5 days) shows acceptable therapeutic efficacy and safety[1].
HDAC1-IN-3 (5 mg/kg; i.p.) shows good pharmacokinetic properties[1].
Pharmacokinetic Parameters of HDAC1-IN-3 in Female BALB/c mice[1].

parameter	JX35
C_{max} (ng/mL)	539
T_{max} (h)	0.25
AUC_{last} (h·ng/mL)	638
AUC_{inf} (h·ng/mL)	640
$t_{1/2}$ (h)	0.91
$CL_{Z/F}$ (L/h/kg)	7.81
$V_{Z/F}$ (L/kg)	10.20

Female BALB/c mice; 5 mg/kg; i.p.

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

Animal Model:	6-8 weeks, BALB/c female mice[1]
Dosage:	30, 60, 90 mg/kg
Administration:	I.p., once daily for 5 days
Result:	Showed acceptable therapeutic efficacy and safety.

Animal Model:	6-8 weeks, female BALB/c mice[1]
Dosage:	5 mg/kg
Administration:	I.p.
Result:	Showed good pharmacokinetic properties.

REFERENCES

[1]. Wang M, et al. Drug Repurposing of Quisinostat to Discover Novel Plasmodium falciparum HDAC1 Inhibitors with Enhanced Triple-Stage Antimalarial Activity and Improved Safety. J Med Chem. 2022; 65(5):4156-4181.

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