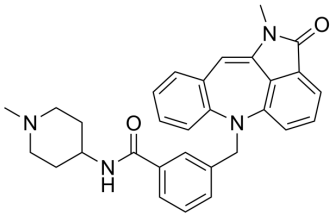
BET BD2-IN-1

Cat. No.:	HY-155680
CAS No.:	2677039-24-4
Molecular Formula:	$C_{30}H_{30}N_4O_2$
Molecular Weight:	478.58
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

BET BD2-IN-1 (compound 45) is a potent and selective inhibitor of BET BD2 (IC_{50}=1.6 nM). BET BD2-IN-1 inhibits the differentiation of Th17 cells by decreasing the activation of STAT3 and NF-κB. BET BD2-IN-1 is used in psoriasis and inflammatory bowel disease (IBD) research[1].

IC_{50} & Target

BRD2 BD1 570 nM (IC_{50})	BRD2 BD2 5.9 nM (IC_{50})	BRD3 BD1 465 nM (IC_{50})	BRD3 BD2 6.0 mM (IC_{50})
BRD4 BD1 524 nM (IC_{50})	BRD4 BD2 1.6 nM (IC_{50})	BRDT BD1 527 nM (IC_{50})	

In Vitro

BET BD2-IN-1 (500 nM) effectively inhibits Th17 cell differentiation and has excellent selectivity for BD2 over BD1[1].

BET BD2-IN-1 (4 nM) binds to BRD4 BD2 in intact cells and has stabilization effect on BRD4 BD2[1].

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

Cell Differentiation Assay[1]

Cell Line:	Th17 cells
Concentration:	500 nM
Incubation Time:	
Result:	Showed the strongest inhibitory activity and reduced differentiation from 19.0 to 7.81%.

Cell Migration Assay [1]

Cell Line:	HEK 293 T cells
Concentration:	4, 20, 100, 500, 2500, 10000 nM
Incubation Time:	30 min
Result:	Stabilized BRD4 BD2 at 50.4 °C.

In Vivo

BET BD2-IN-1 (20 mg/kg for i.v; once daily for seven days) inhibits the protein expression of p-STAT3 and p-NF-κB in mouse skin tissues, effectively ameliorates the pathological changes in the psoriasis mouse model[1].
BET BD2-IN-1 (20 mg/kg for i.v; once daily for seven days) significantly decreases the disease activity index (DAI) score in dextran sulfate sodium (DSS) induced IBD mouse model[1].
Pharmacokinetic Analysis of BET BD2-IN-1 in Sprague Dawley Rats Model[1]

parameter	AUC(0-t) (ng•h/mL)	C0 (ng/mL)	T1/2 (h)	CL (mL/kg/min)	Vdss (L/kg)
iv(1 mg/kg)	272 ± 7.2	279 ± 78	1.5 ± 0.1	60 ± 2.0	6.6 ± 0.8

parameter	AUC(0-t) (ng•h/mL)	Cmax (ng/mL)	T1/2 (h)	Tmax (h)	F (%)
po(10 mg/kg)	78 ± 34	20 ± 11	1.9 ± 0.2	2.7 ± 1.2	2.9 ± 1.2

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

Animal Model:	Imiquimod (HY-B0180)-induced Psoriasis mouse model[1]
Dosage:	10 and 20 mg/kg
Administration:	Intravenous injection (i.v.) ; Once daily for seven days
Result:	Significantly alleviated the Imiquimod-induced skin lesions in a dose-dependent manner. Obviously reduced the enlarged spleen. Significantly decreased the expression of p-STAT3 and p-NF-κB in mouse skin tissues.

Animal Model:	DSS (HY-116282C)-induced IBD mouse model[1]
Dosage:	10 and 20 mg/kg
Administration:	Intravenous injection (i.v.) ; Once daily for seven days
Result:	Effectively prevented colon shortening. Effectively alleviated the DSS-induced weight loss. Significantly alleviated the infiltration of inflammatory cells, areas of ulceration as well as loss of mucosal epithelium, and goblet cells caused by DSS.

REFERENCES

[1]. Wang Z, et al. Discovery of a Bromodomain and Extra Terminal Domain (BET) Inhibitor with the Selectivity for the Second Bromodomain (BD2) and the Capacity for the Treatment of Inflammatory Diseases. J Med Chem. 2023 Aug 10;66(15):10824-10848.

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