PROTAC BRD3/BRD4-L degrader-2

Cat. No.: HY-149948

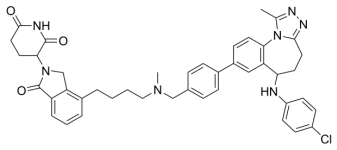
Molecular Formula: $C_{43}H_{44}ClN_7O_3$

Molecular Weight: 742.31

Target: Epigenetic Reader Domain; PROTACs

Pathway: Epigenetics; PROTAC

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



BIOLOGICAL ACTIVITY

Description

PROTAC BRD3/BRD4-L degrader-2 is a PROTAC molecule and can selectively degrade cellular BRD3 and BRD4-L with K_i values of 16.91 and 2.8 nM, respectively. PROTAC BRD3/BRD4-L degrader-2 also has robust antitumor activity in mouse xenograft models. PROTAC BRD3/BRD4-L degrader-2 can be used for the research of cancer[1].

IC_{50} & Target

Ki: 16.91 nM (BRD3 BD1); 2.8 nM (BRD3 BD2) [1].
IC50: 7.46 nM (MV4-11 cells); 85.4 nM (MM.1 S cells) [1].

In Vitro

PROTAC BRD3/BRD4-L degrader-2 (Compound 28) has binding affinity for BRD3 BD1and BRD3 BD2 with K_i values of 16.91 and 2.8 nM, respectively[1].
PROTAC BRD3/BRD4-L degrader-2 has cellular activity in MV4-11 and MM.1 S cell lines with IC_{50} values of 7.46 and 85.4 nM, respectively[1].
PROTAC BRD3/BRD4-L degrader-2 (30 nM; 1, 3, 6, 8, 24 h) has a selective degradation effect for BRD3 and BRD4-L in a time-dependent manner[1].
PROTAC BRD3/BRD4-L degrader-2 (1, 3, 10, 30, 100, 300 nM; 24 h) has antitumor activity in MM.1 S cells and dosedependently induced cell cycle arrest at G1 phase[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	MM.1 S cells
Concentration:	30 nM
Incubation Time:	1, 3, 6, 8, 24 h
Result:	Degraded BRD3 and BRD4-L in a time-dependent manner.

In Vivo

PROTAC BRD3/BRD4-L degrader-2 (compound 28) (oral, i.v.; 3 mg/kg) has poor oral bioavailability and shows good systemic exposure when administered intravenously[1].
PROTAC BRD3/BRD4-L degrader-2 (i.v.; 3 mg/kg) has antitumor efficacy in MM.1 S mouse xenograft model[1].
PROTAC BRD3/BRD4-L degrader-2 (i.v.; 1, 5 mg/kg; signal dose) promotes selective degradation of BRD3 and BRD4-L in vivo and exhibits robust antitumor activity[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57 mice[1].
Dosage:	3 mg/kg
Administration:	Oral gavage; Intravenous injection
Result:	

	T_{max} (h)	$T_{1/2}$(h)	C_{max} (ng/mL)	AUC_{0-t} (h×ng/mL)	CL (mL/h/kg)	F(%)
i.v. 3 mg/kg	0.1	0.5	7414 ± 1765	2961 ± 314	1016 ± 114	
p.o. 3 mg/kg	0.4 ± 0.1	na	51 ± 23	26 ± 8	74130 ± 44731	2.14

Animal Model:	MM.1S mouse xenograft model[1].
Dosage:	1, 5 mg/kg
Administration:	i.v.; signal dose
Result:	Inhibited tumor growth with 40% at 1 mg/kg and shows 64% tumor growth inhibition at 5 mg/kg. Promoted selectively depletion of BRD3 and BRD4-L in tumor tissue for 1 mg/kg and 5 mg/kg.

REFERENCES

[1]. Yan Z, et al. Selective degradation of cellular BRD3 and BRD4-L promoted by PROTAC molecules in six cancer cell lines. Eur J Med Chem. 2023;254:115381.

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