BRD4/NAMPT-IN-1

Cat. No.: HY-161515

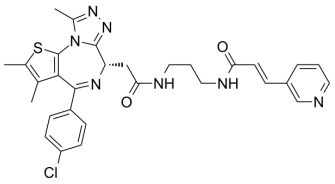
Molecular Formula: $C_{30}H_{30}ClN_7O_2S$

Molecular Weight: 588.12

Target: NAMPT; Epigenetic Reader Domain

Pathway: Metabolic Enzyme/Protease; Epigenetics

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



BIOLOGICAL ACTIVITY

Description

BRD4/NAMPT-IN-1 (Compound A2) shows strong inhibitory effects on NAMPT and BRD4 (IC_{50}=35 nM (NAMPT) and 58 nM (BRD4)). BRD4/NAMPT-IN-1 inhibits the growth and migration of hepatocellular carcinoma cells and promotes apoptosis. BRD4/NAMPT-IN-1 also shows potent anticancer effects in HCCLM3 xenograft mouse model, with no obvious toxic effects[1].

IC_{50} & Target

BRD4(BD1BD2)	BRD4 (BD1)	BRD4 (BD2)
58 nM (IC_{50})	12 nM (IC_{50})	41 nM (IC_{50})

In Vitro

BRD4/NAMPT-IN-1 exhibits IC_{50} values of 12 nM for BRD4(BD1) and 41 nM for BRD4(BD2) against other members of the BET family[1].BRD4/NAMPT-IN-1 inhibits the proliferation of cancer cells with IC_{50} of 2.37 μM (Hep3B), 6.49 μM (Huh7), 5.44 μM (HCCLM3) and 9.51 μM (LX-2), respectively[1].

BRD4/NAMPT-IN-1 (1-10 μM; 72 h) on Hep3B cells shows that: 1: it can inhibit the expression of oncogenes up-regulated by BRD4, and at the same time reduces the levels of NAPRT and NAMPT. 2: It significantly increases cell arrest at G0/G1 phase. 3: It dose-dependently induces apoptosis. 4: It dose-dependently inhibits the migratory ability of the cells[1].

BRD4/NAMPT-IN-1 (1-10 μM; 72 h) dose-dependently reduces NAD^+ concentration in Hep3B cells and HCCLM3 cells[1].

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

Apoptosis Analysis[1]

Cell Line:	Hep3B cells
Concentration:	1; 5; 10 μM
Incubation Time:	72 h
Result:	The apoptosis rate induced was significantly higher than that of the control FK866 (HY-50876) and JQ1 (HY-13030) at the same dose.

Cell Cycle Analysis[1]

Cell Line:	Hep3B cells
Concentration:	1; 5; 10 μM
Incubation Time:	72 h
Result:	Significantly increased the accumulation of Hep3B cells at the G0/G1 stage over the

	commonly used hepatocellular carcinoma therapeutic agents FK866 (HY-50876) and JQ1 (HY-13030).

In Vivo

BRD4/NAMPT-IN-1 (i.p.; 40 mg/kg/day and 80 mg/kg/day; 27 days) exhibits dose-dependent tumor suppression in HCCLM3 xenograft nude mice[1].

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

Animal Model:	HCCLM3 xenograft nude mice [1]
Dosage:	40 mg/kg/day and 80 mg/kg/day
Administration:	i.p.; 27day
Result:	Inhibited the growth of HCCLM3 tumors significantly in both groups at two different doses, with significant decreases in tumor volume and weight. In the 40 mg/kg dose group, the tumor growth inhibition rate reached 37.20%, and in the 80 mg/kg dose group, the tumor growth inhibition rate reached 58.17%. Showed no significant weight loss or other significant toxic side effects.

REFERENCES

[1]. Yin C, et al. Discovery of potent and novel dual NAMPT/BRD4 inhibitors for efficient treatment of hepatocellular carcinoma. Eur J Med Chem. 2024 May 5;271:116444.

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