BETd-260

Cat. No.: HY-101519

CAS No.: 2093388-62-4

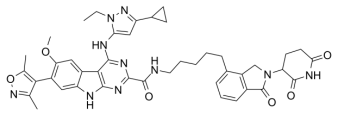
Molecular Formula: $C_{43}H_{46}N_{10}O_6$

Molecular Weight: 799

Target: PROTACs; Epigenetic Reader Domain; Apoptosis

Pathway: PROTAC; Epigenetics; Apoptosis

Storage: -80°C, protect from light, stored under nitrogen



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (31.29 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2516 mL	6.2578 mL	12.5156 mL
	5 mM	0.2503 mL	1.2516 mL	2.5031 mL
	10 mM	0.1252 mL	0.6258 mL	1.2516 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.83 mg/mL (1.04 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.83 mg/mL (1.04 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BETd-260 (ZBC 260) is a PROTAC connected by ligands for Cereblon and BET, with as low as 30 pM against BRD4 protein in RS4;11 leukemia cell line[1]. BETd-260 potently suppresses cell viability and robustly induces apoptosis in hepatocellular carcinoma (HCC) cells[2].

IC_{50} & Target

BRD4	BRD2	BRD3
<30 pM (IC_{50})	30-100 pM (IC_{50})	30-100 pM (IC_{50})

In Vitro

BETd-260 (ZBC260; Compound 23) is capable of inducing degradation of BRD2, BRD3, and BRD4 proteins at 30–100 pM in the RS4;11 leukemia cells. BETd-260 shows inhibitory activity against the growth of RS4;11 leukemia cells and MOLM-13 cells with IC_{50}s of 51 pM and 2.2 nM, respectively, and induces apoptosis in both RS4;11 and MOLM-13 cell lines at 3-10 nM[1]. BETd-260 reciprocally modulates the expression of several apoptotic genes in HCC cells, i.e., suppressing the expression of

	anti-apoptotic Mcl-1, Bcl-2, c-Myc, and XIAP, whereas increasing the expression of pro-apoptotic Bad[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BETd-260 (5 mg/kg, i.v., every other day, thrice a week for 3 weeks) causes rapid tumor regression with a maximum of >90% regression in mice bearing RS4;11 xenograft tumors, and with no body weight loss or other signs of toxicity in mice. BETd-260 (5 mg/kg, i.v.) degrades the BRD2, BRD3, and BRD4 proteins for more than 24 h, with robust cleavage of PARP and caspase-3, and strong down-regulation of c-Myc protein in RS4;11 xenograft mice model[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	In cell growth experiments, cells are seeded in 96-well cell culture plates at a density of 10000−20000 cells/well in 100 µL of culture medium. BETd-260 is serially diluted in the appropriate medium, and 100 µL of the diluted solution containing BETd-260 is added to the appropriate wells of the cell plate. After addition of BETd-260, the cells are incubated for 4 days at 37°C in an atmosphere of 5% CO_2. Cell growth is evaluated by a lactate dehydrogenase-based WST-8 assay using a multimode microplate reader. The WST-8 reagent is added to the plate, incubated for at least 1 h, and read at 450 nm. The readings are normalized to the DMSO-treated cells, and the IC_{50} is calculated by nonlinear regression analysis using GraphPad Prism 6 software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] To develop xenograft tumors, 5×10^6 RS4;11 cells with 50% Matrigel are injected subcutaneously on the dorsal side of severe combined immunodeficient (SCID) mice, one tumor per mouse. When tumors reach appr 100 mm^3, mice are randomly assigned to BETd-260 treatment and vehicle control groups. Animals are monitored daily for any signs of toxicity and weighed 2-3 times per week during the treatment and weighed at least weekly after BETd-260 treatment end. Tumor size is measured 2-3 times per week by electronic calipers during the treatment period and at least weekly after the treatment is end. Tumor volume is calculated as $V = LW^2/2$, where L is the length and W is the width of the tumor[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Zhou B, et al. Discovery of a Small-Molecule Degrader of Bromodomain and Extra-Terminal (BET) Proteins with Picomolar Cellular Potencies and Capable of Achieving Tumor Regression. J Med Chem. 2018 Jan 25;61(2):462-481.

[2]. Zhang H, et al. Targeting BET Proteins With a PROTAC Molecule Elicits Potent Anticancer Activity in HCC Cells. Front Oncol. 2020;9:1471. Published 2020 Jan 14.

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