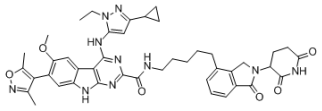
BETd-260

Cat. No.:	HY-101519
CAS No.:	2093388-62-4
Molecular Formula:	$C_{43}H_{46}N_{10}O_6$
Molecular Weight:	798.89
Target:	PROTAC; Epigenetic Reader Domain
Pathway:	PROTAC; Epigenetics
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (**31.29 mM;** Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.2517 mL	6.2587 mL	12.5174 mL
5 mM	0.2503 mL	1.2517 mL	2.5035 mL
10 mM	0.1252 mL	0.6259 mL	1.2517 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 is a potent **BET** degrader based on **PROTAC** technology, with as low as 30 pM against **BRD4** protein in RS4;11 leukemia cell line.

IC_{50} & Target

BRD4[1]
PROTAC

In Vitro

BETd-260 (ZBC260; Compound 23) 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].

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].

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.

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