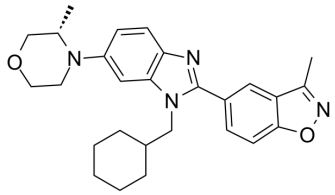
Y06137

Cat. No.:	HY-111503
CAS No.:	2226534-49-0
Molecular Formula:	$C_{27}H_{32}N_4O_2$
Molecular Weight:	444.57
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 62.5 mg/mL (140.59 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2494 mL	11.2468 mL	22.4936 mL
	5 mM	0.4499 mL	2.2494 mL	4.4987 mL
	10 mM	0.2249 mL	1.1247 mL	2.2494 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: ≥ 2.08 mg/mL (4.68 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Y06137 is a potent and selective BET inhibitor for treatment of castration-resistant prostate cancer (CRPC). Y06137 binds to the BRD4(1) bromodomain with a K_d of 81 nM[1].

IC_{50} & Target

BRD4(1)
81 nM (Kd)

In Vitro

Y06137 (0.001-100 nM, 96 hours for LNCaP, C4-2B, and 22Rv1 cells; 144 hours for VCaP cells) exhibits low micromolar or nanomolar potencies (IC_{50}: 0.29-2.6 μM) in the four androgen receptor (AR)-positive prostate cancer cell lines LNCaP, C4-2B, 22Rv1, and VCaP. Treatment of 22Rv1 cells with Y06137 (1, 2, 4, 8, and 16 μM, 48 hours) results in significant down-regulation of both full-length (AR-fl) and AR variants levels[1].

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

Cell Viability Assay[1]

Cell Line:	AR-positive prostate cancer cell lines LNCaP, C4-2B, 22Rv1, and VCaP
Concentration:	0.001-100 μM
Incubation Time:	96 hours for LNCaP, C4-2B, and 22Rv1; 144 hours for VCaP
Result:	Inhibited LNCaP, C4-2B, 22Rv1, and VCaP cells with IC_{50}s of 0.47, 0.84, 0.70, 0.29 μM, respectively.

Western Blot Analysis[1]

Cell Line:	AR-positive prostate cancer cell lines 22Rv1
Concentration:	1, 2, 4, 8, and 16 μM
Incubation Time:	48 hours
Result:	Resulted in significant down-regulation of both AR-fl and AR variants levels.

In Vivo

Y06137 (50 mg/kg, i.p. injection, 5 times per week, 25 days) demonstrates therapeutic effects in a C4-2B CRPC xenograft tumor model in mice. Y06137 is well tolerated in the treated mice, based on the weight of the animal body and their general behavior[1].

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Animal Model:	Four-week-old male mice (strain: C.B-17/IcrHsd-Prkdc^{scid} for C4-2B) with C4-2B mouse xenograft model[1]
Dosage:	50 mg/kg, 100 μL
Administration:	Intraperitoneal (i.p.) injection, 5 times per week, 25 days
Result:	Exhibited strong antitumor activities during the 25-day treatment period, with a tumor growth inhibition (TGI) of 51%.

REFERENCES

[1]. Zhang M, et al. Structure-Based Discovery and Optimization of Benzo[d]isoxazole Derivatives as Potent and Selective BET Inhibitors for Potential Treatment of Castration-Resistant Prostate Cancer (CRPC). J Med Chem. 2018 Apr 12;61(7):3037-3058.

Caution: Product has not been fully validated for medical applications. For research use only.

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