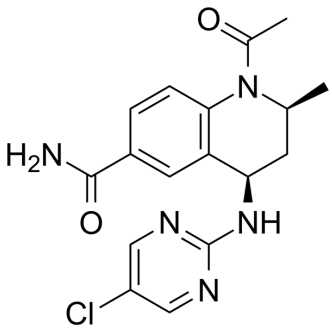
I-BET567

Cat. No.:	HY-142520
CAS No.:	1887237-54-8
Molecular Formula:	$C_{17}H_{18}ClN_5O_2$
Molecular Weight:	359.81
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (277.92 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7792 mL	13.8962 mL	27.7924 mL
	5 mM	0.5558 mL	2.7792 mL	5.5585 mL
	10 mM	0.2779 mL	1.3896 mL	2.7792 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: ≥ 2.5 mg/mL (6.95 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.95 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.95 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

I-BET567 is a potent and orally active inhibitor of pan-BET candidate with pIC_{50}s of 6.9 and 7.2 for BRD4 BD1 and BD2, respectively. I-BET567 has been demonstrated efficacy in mouse models of oncology and inflammation[1].

IC_{50} & Target

BRD4 (BD1)	BRD2
6.9 (pIC_{50})	7.2 (pIC_{50})

In Vitro

I-BET567 (compound 27) (72 hours; 1.5 nM-30 μM) effectively inhibites the proliferation of human NMC cell line 11060 in vitro with a mean $gpIC_{50}$ 6.2 (0.63 μM)[1].

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

Cell Viability Assay[1]

Cell Line:	NMC line 11060 cells
Concentration:	1.5 nM-30 μM
Incubation Time:	72 hours
Result:	Significantly reduced cell growth.

In Vivo

I-BET567 (compound 27) (3, 10, and 30 mg/kg; p.o.; once daily for 20 days) leads to a significant reduction in tumor growth compared with vehicle controls at both 10 and 30 mg/kg[1].

Assessment of Pharmacokinetics (PK) profile of I-BET567 following intravenous infusion and oral administration in male wistar han rat and beagle dog[a][1].

species	dose iv[b] /po[c] (mg/kg)	CL^{b} (mL/min/kg)	$CL^{b,u}$ (mL/min/kg)	CL^{renal} (mL/min/kg)	V_{ss} (L/kg)	$V_{ss,u}$ (L/kg)	$t_{1/2}$ (h)	Fpo (%)	f_{ub}
rat	1.3/3	25	109	7	2.4	10.4	1.6	99[d]	0.23
dog	1.0/3	8.1	20	6.9	1.2	2.9	1.8	98	0.41

a: Values are mean, n=3 unless otherwise stated. b: IV dose 1h infusion in DMSO and (10%, w/v) Kleptose HPB in saline (2%: 98% (v/v)). c: PO dose vehicle: 1%(w/v) methycellulose (400 cps) (aq). d: Mean n = 2.

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

Animal Model:	NMC 11060 xenograft mouse model (NOD/SCID mouse; bearing NMC 11060 cells) [1]
Dosage:	3, 10, and 30 mg/kg
Administration:	p.o. (once daily for 20 days
Result:	Led to a significant reduction in tumor growth compared to vehicle controls at both 10 and 30 mg/kg.

REFERENCES

[1]. Humphreys PG, et al. Design, Synthesis, and Characterization of I-BET567, a Pan-Bromodomain and Extra Terminal (BET) Bromodomain Oral Candidate [published online ahead of print, 2022 Jan 7].

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