I-BET151

Cat. No.: HY-13235

CAS No.: 1300031-49-5

Molecular Formula: $C_{23}H_{21}N_5O_3$

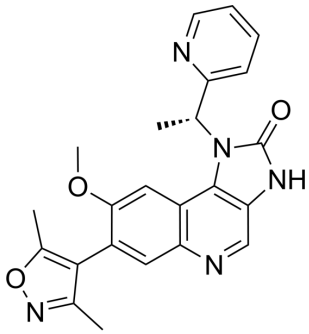
Molecular Weight: 415.44

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 : ≥ 100 mg/mL (240.71 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4071 mL	12.0354 mL	24.0709 mL
5 mM	0.4814 mL	2.4071 mL	4.8142 mL
10 mM	0.2407 mL	1.2035 mL	2.4071 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 (6.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.02 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.02 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (6.02 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.02 mM); Clear solution
6. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: 0.5 mg/mL (1.20 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description	I-BET151 (GSK1210151A) is a BET bromodomain inhibitor which inhibits BRD4, BRD2, and BRD3 with pIC_{50} of 6.1, 6.3, and 6.6, respectively[1][2].
IC_{50} & Target	pIC50: 6.1 (BRD4), 6.3 (BRD2), 6.6 (BRD3)[1]

In Vitro

I-BET151 (1 μM; 72 hours) treatment displays the majority of live cells resided in the G_0 phase and commensurate with a dose- and time-dependent decrease in cell proliferation and abrogation of bromodeoxyuridine incorporation[2].
?I-BET151 (100 nM; 72 hours) causes a significant dose- and time-dependent decrease in the proportion of myeloma cells in S/G_2 phase[2].

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

Cell Viability Assay[2]

Cell Line:	H929 cells
Concentration:	1 μM
Incubation Time:	72 hours
Result:	Displays the majority of live cells resided in the G_0 phase and commensurate with a dose- and time-dependent decrease in cell proliferation and abrogation of bromodeoxyuridine incorporation.

Cell Proliferation Assay[2]

Cell Line:	H929 cells
Concentration:	100 nM
Incubation Time:	72 hours
Result:	Caused a significant dose- and time-dependent decrease in the proportion of myeloma cells in S/G_2 phase.

In Vivo

I-BET151 demonstrates low blood clearance in the rat (~20% liver blood flow) and good oral systemic exposure which resulted in good oral bioavailability. High clearance is observed in the dog (~95% liver blood flow). The systemic exposure in the dog is low, resulting in a poor oral bioavailability of 16%. The high blood clearance in dog correlates well with the high intrinsic clearance observed in dog microsomes and hepatocytes, whereas the low intrinsic clearances seen in rat and mouse (mouse IVC 1.6 mL/min/g; CLb 8 mL/min/kg) correlate with lower in vivo blood clearances in these species. Due to the low systemic exposure observed in the dog, I-BET151 is investigated in the mini-pig as a potential second species for toxicological evaluation where it showed low clearance (~32% liver blood flow) and good bioavailability (65%)[1].
?I-BET151 (30 mg/kg; i.p.; daily for 21 days)-treats mice has four- to five fold smaller myeloma tumors and a significantly reduces rate of tumor size doubling than vehicle-treated mice[2].

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

Animal Model:	Mice (model of subcutaneous myeloma)[2]
Dosage:	50 mg/kg
Administration:	I.p.; daily for 21 days
Result:	Reduced rate of tumor size doubling than vehicle-treated mice.

CUSTOMER VALIDATION

- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Cell Stem Cell. 2021 Sep 2;28(9):1597-1613.e7.
- Cell Syst. 2018 Apr 25;6(4):424-443.e7.
- Oncogene. 2021 Apr;40(15):2711-2724.
- J Transl Med. 2022 Jul 28;20(1):336.

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REFERENCES

[1]. Seal J, et al. Identification of a novel series of BET family bromodomain inhibitors: Binding mode and profile of I-BET151 (GSK1210151A). Bioorg Med Chem Lett. 2012 Apr 15;22(8):2968-72.

[2]. Chaidos A, et al. Potent antimyeloma activity of the novel bromodomain inhibitors I-BET151 and I-BET762. Blood. 2014 Jan 30;123(5):697-705.

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