产品名称：I-BET151
产品别名：I-BET151

生物活性：

Description	I-BET151 is a **BET bromodomain** inhibitor which inhibits **BRD4**, **BRD2**, and **BRD3** with **pIC$_{50}$** of 6.1, 6.3, and 6.6, respectively.
IC$_{50}$ & Target	pIC50: 6.1 (BRD4), 6.3 (BRD2), 6.6 (BRD3)[1]
In Vitro	I-BET151 (GSK1210151A) causes a significant dose- and time-dependent decrease in the proportion of myeloma cells in S/G$_2$ phase at 24, 48, and 72 hours. The most pronounced effect is observed at 72 hours in all 6 myeloma cell lines, starting at 100 nM. Dual Ki67/propidium iodide staining confirmed that the majority of live cells resided in the G$_0$ phase after treatment with I-BET151 at 1 μM for 72 hours commensurate with a dose- and time-dependent decrease in cell proliferation and abrogation of bromodeoxyuridine incorporation[2].
In Vivo	I-BET151 (GSK1210151A) 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]. In an in vivo model of subcutaneous myeloma, I-BET151 (50 mg/kg)-treated mice has four- to five fold smaller myeloma tumors (P<0.001) and a significantly reduced rate of tumor size doubling than vehicle-treated mice (P<0.001)[2].
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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

	Solubility: ≥ 2.5 mg/mL (6.02 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.02 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.02 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.02 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.02 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.02 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	For in vitro cell proliferation and apoptosis assays, myeloma cell lines are cultured by using RPMI 1640 medium supplemented with 10% fetal bovine serum, and 2 mM L-glutamine. Cells are placed in 96-well U-bottom plates at final concentration of 0.2×10^6 cells per milliliter in a humidified incubator with 5% CO_2 at 37°C. For stroma vs nonstroma experiments, myeloma cells are placed in flat-bottom 96-well plates with MS5 cells at >90% confluence or in wells without stroma. Compounds (ie, I-BET151, I-BET762, the inactive isomer I-BET768, and JQ1) are serially diluted into media and added to the cultures at the indicated concentrations, starting from a 10-mM DMSO stock solution. Primary myeloma cells are cultured in flat-bottom 96-well plates in the presence of MS5 stroma cells by using complete medium as above, supplemented with interleukin-6 (IL-6) at 5 ng/mL[2].
Animal Administration	Mice[2] NOD.Cg-Prkdcscid Il2rgtm1Wjl/SzJ (NSG) mice are used. In total, 5×10^6 KMS11 myeloma cells are injected subcutaneously into 9- to 12-week-old NSG mice. When tumors are ≥5 mm in maximum diameter, mice are randomized to receive once daily intraperitoneal injection of either I-BET151 30 mg/kg in 0.9% NaCl plus Kleptose hydroxypropyl betadex 10% (w/v) and DMSO 5% (v/v) pH 5.0 or vehicle solution for a maximum of 21 days.
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.