

产品名称: **BI-9564**

产品别名: **BI-9564**

生物活性:				
Description	BI-9564 is a potent, selective and cell-permeable BRD9/BRD7 bromodomains inhibitor, with IC50s of 75 nM and 3.4 μ M and Kds of 14 nM and 239 nM, respectively. BI-9564 has an IC50 of > 100 μ M for BET family[1].			
IC ₅₀ & Target	BRD9	BRD9	BRD7	BRD7
	75 nM (IC ₅₀)	14 nM (Kd)	3.4 μ M (IC ₅₀)	239 nM (Kd)
In Vitro	BI-9564 (<5 μ M) shows no activity against 324 kinases, and at 10 μ M, an inhibition >40% is observed for only 2 out of 55 GPCRs. BI-9564 has antiproliferative effect on human acute myeloid eosinophilic leukemia cell line EOL-1, with EC50 of 800 nM[1]. BI-9564 shows Kd of 73 nM for BRD7, and is >10-fold more selective for BRD9 over the highly homologues bromodomain BRD7, which has been implied as a tumor suppressor and is down-regulated in cancer cells[2].			
In Vivo	BI-9564 (180 mg/kg, p.o.) shows attractive ADME/PK profiles for in vivo proof-of-concept studies. BI-9564 results in a modest but significant additional survival benefit of 2 days compared to survival of the control group in a xenograft model of human AML[1].			
Solvent&Solubility	In Vitro: DMSO : 8.33 mg/mL (23.57 mM; Need ultrasonic)			
	Preparing Stock Solutions	<div>Solvent / Mass / Concentration</div>	1 mg	5 mg
		1 mM	2.8296 mL	14.1479 mL
		5 mM	0.5659 mL	2.8296 mL
		10 mM	0.2830 mL	1.4148 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℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用，-20℃ 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: ≥ 0.83 mg/mL (2.35 mM); Clear solution 此方案可获得 ≥ 0.83 mg/mL (2.35 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μ L 8.3 mg/mL 的澄清 DMSO 储备液加到 400 μ L PEG300 中，混合均匀； 向上述体系中加入 50 μ L Tween-80，混合均匀；然后继续加入 450 μ L 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: ≥ 0.83 mg/mL (2.35 mM); Clear solution 此方案可获得 ≥ 0.83 mg/mL (2.35 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μ L 8.3 mg/mL 的澄清 DMSO 储备液加到 900 μ L 20% 的 SBE- β -CD 生理			

	<p>盐水水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 0.83 mg/mL (2.35 mM); Clear solution</p> <p>此方案可获得 ≥ 0.83 mg/mL (2.35 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。</p> <p>以 1 mL 工作液为例，取 100 μL 8.3 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p>
References	<p>[1]. Martin LJ, et al. Structure-Based Design of an in Vivo Active Selective BRD9 Inhibitor. J Med Chem. 2016 May 26;59(10):4462-75.</p> <p>[2]. Rezaul M. Karim, et al. An Advanced Tool To Interrogate BRD9. J. Med. Chem., 2016, 59 (10), pp 4459-4461</p>
实验参考：	
Cell Assay	<p>Cells are grown in 50 μL medium as specified by the supplier for 7 days starting with 500 and with 1000 cells per well of a 384 well plate in the presence of varying concentrations of compound before measuring viability via cellular ATP levels using the cell titer glow assay. [1]</p>
Animal Administration	<p>Female CIEA-NOG mice are engrafted intravenously with 1×10^7 EOL-1 AML cells stably expressing luciferase and GFP. Following injection of the cells animals are randomized based on body weight ($n=10/\text{group}$). Treatment starts on day 5 with either 0.5% Natrosol or BI-9564 formulated with 0.5% Natrosol. All doses are calculated relative to the mouse body weight on the treatment day. BI-9564 and the vehicle control are administered orally with a dosing volume of 10 mL/kg body weight. BI-9564 is administered daily from day 5 until 17 and from day 20 until 22. Dosing is interrupted on day 18 for two days as one mouse in the treatment group reaches -15% body weight loss. Tumour load is measured 2-3 times weekly based on bioluminescence imaging. The following scoring system is used: score 0, no clinical signs; score 1, tail or hind limb weakness. Animals are sacrificed based on severity criteria including appearance of paralysis score 1 and/or body weight loss exceeding -18%. In S54 this tumor mouse model body weight changes can occur due to increased tumor load or due to intolerability. [1]</p>
References	<p>[1]. Martin LJ, et al. Structure-Based Design of an in Vivo Active Selective BRD9 Inhibitor. J Med Chem. 2016 May 26;59(10):4462-75.</p> <p>[2]. Rezaul M. Karim, et al. An Advanced Tool To Interrogate BRD9. J. Med. Chem., 2016, 59 (10), pp 4459-4461</p>