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产品名称: **GNE-272**  
产品别名: **GNE-272**

生物活性:				
Description	GNE-272 is a potent and selective <i>in vivo</i> probe for the bromodomains of CBP/EP300 with IC <sub>50</sub> values of 0.02, 0.03 and 13 μM for CBP, EP300 and BRD4, respectively.			
IC <sub>50</sub> & Target	IC <sub>50</sub> : 0.02 μM (CBP), 0.03 μM (EP300), 13 μM (BRD4) <sup>[1]</sup>			
In Vitro	GNE-272 is exquisitely selective for CBP/ EP300 and remarkably selective (650-fold) over BRD4. When tested at 10 μM in 35 kinase panel and 42 receptors off-target screening panel, GNE-272 does not inhibit any target at >30%. In addition, GNE-272 does not inhibit (>10 μM, top concentration) several cytochrome P450s (3A4, 1A2, 2C9, 2C19, 2D6). The compound has good potency in the BRET cellular assay. In an orthogonal measure of the target engagement, GNE-272 is shown to inhibit the expression of MYC10 (MV4-11 cell line) with an EC <sub>50</sub> of 0.91 μM and good correlation between the BRET and MYC cellular assays is observed <sup>[1]</sup> .			
In Vivo	GNE-272 demonstrates low clearance following a 1 mg/ kg intravenous dose in a mouse PK experiment and good oral bioavailability when dosed at 100 mg/kg, reaching an unbound C <sub>max</sub> of 26 μM. GNE-272 shows a marked antiproliferative effect in hematologic cancer cell lines and modulates MYC expression <i>in vivo</i> that corresponds with antitumor activity in an AML tumor model <sup>[1]</sup> .			
Solvent&Solubility	<b>In Vitro:</b> DMSO : 100 mg/mL (235.59 mM; Need ultrasonic)			
		Solvent Concentration	Mass	
	Preparing	1 mM	2.3559 mL	11.7794 mL
	Stock Solutions	5 mM	0.4712 mL	2.3559 mL
		10 mM	0.2356 mL	1.1779 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。 <b>In Vivo:</b> 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 (5.89 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.89 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。			



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	<p>2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2.5 mg/mL (5.89 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.89 mM, 饱和度未知) 的澄清溶液。</p> <p>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: ≥ 2.5 mg/mL (5.89 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.89 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。</p>
References	[1]. Crawford TD, et al. Discovery of a Potent and Selective in Vivo Probe (GNE-272) for the Bromodomains of CBP/EP300. J Med Chem. 2016 Dec 8;59(23):10549-10563.
实验参考:	
Cell Assay	Human cancer cell lines (MOLM-16, HL-60, LP-1, KMS-34, Pfeiffer, DOHH-2) are treated for 4 h with 5 μM GNE-272 or DMSO control. After 6 days, cell viability is measured by CellTiter-Glo[1].
Animal Administration	Mice: Mice are given 0 (vehicle, 0.5% methylcellulose; 0.2% Tween-80), 12.5, 25, and 50 mg/kg of GNE-272 by gavage, twice daily (BID) for 21 days in a volume of 100 μL. Tumor volumes are measured in two dimensions (length and width) using Ultra CalIV calipers and analyzed using Excel, version 11.2[1].
References	[1]. Crawford TD, et al. Discovery of a Potent and Selective in Vivo Probe (GNE-272) for the Bromodomains of CBP/EP300. J Med Chem. 2016 Dec 8;59(23):10549-10563.

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