

产品名称: **Evacetrapib (LY2484595)**

产品别名: **Evacetrapib**

生物活性:				
Description	Evacetrapib is a potent and selective of CETP inhibitor, which inhibits human recombinant CETP protein (IC₅₀ 5.5 nM) and CETP activity in human plasma (IC₅₀ 36 nM) in vitro.			
IC ₅₀ & Target	IC50: 5.5 nM (CETP)[1]			
In Vitro	Evacetrapib is a novel benzazepine-based CETP inhibitor. In the buffer CETP assay, the absolute potency of the compound is 5.5 nM. In the human plasma CETP assay, the CETP concentration is about 2 µg/mL (25 nM) and the 36 nM IC50 value again indicates that Evacetrapib is a potent CETP inhibitor against either the recombinant protein or CETP from human plasma. Evacetrapib is apparently much more potent than Dalcetrapib[1].			
In Vivo	In double transgenic mice expressing human CETP and apoAII, Evacetrapib exhibits an ex vivo CETP inhibition ED50 of less than 5 mg/kg at 8 h post oral dose and significantly elevated HDL cholesterol. Importantly, no blood pressure elevation is observed in rats dosed with Evacetrapib at high exposure multiples compared with the positive control, torcetrapib. Evacetrapib administered orally at 30 mg/kg results in 98.4%, 98.6%, and 18.4% inhibition of CETP activity at 4, 8 and 24 h post dose respectively. Evacetrapib dosed orally at 30 mg/kg resulted in 129.7% increase in HDL-C 8 h after oral administration[1].			
Solvent&Solubility	In Vitro: DMSO : ≥ 100 mg/mL (156.58 mM) H₂O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown.			
	Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg
		1 mM	1.5658 mL	7.8290 mL
		5 mM	0.3132 mL	1.5658 mL
		10 mM	0.1566 mL	0.7829 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 <div>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</div> <div>Solubility: ≥ 2.5 mg/mL (3.91 mM); Clear solution</div> <div>此方案可获得 ≥ 2.5 mg/mL (3.91 mM, 饱和度未知) 的澄清溶液。</div> <div>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。</div>			

	<p>2.请依序添加每种溶剂： 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (3.91 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (3.91 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	<p>[1]. Cao G, et al. Evacetrapib is a novel, potent, and selective inhibitor of cholesteryl ester transfer protein that elevates HDL cholesterol without inducing aldosterone or increasing blood pressure. J Lipid Res. 2011 Dec;52(12):2169-76.</p>
实验参考：	
Animal Administration	<p>Rats[1]</p> <p>The blood pressure study is carried out using telemetered, male, obese Zucker Diabetic rats (ZDF fa/fa rats, 8 weeks of age on arrival; n=4). All rats underwent surgical implantation of a telemetry transmitter for continuous monitoring of hemodynamic parameters throughout the study. The rats are acclimated on Purina 5008 chow and house water ad libitum until 11 weeks of age. Mean daily blood pressure for the 24-h period immediately prior to administration of compound is taken as the baseline blood pressure. On the day of an experiment, a single 160 mg/kg dose (in 10% acacia) of Evacetrapib as the lysine salt is administered by oral gavage, and the drug effect is taken as the average daily mean arterial pressure (MAP) during the 24 h period following the dose. Data are expressed as the change in MAP from baseline. Following the last day of blood pressure monitoring, samples are collected from the orbital sinus at 1, 2, 4, 8, and 24 h post dose into tubes containing EDTA and processed into plasma. Plasma concentrations of Evacetrapib are measured using liquid chromatography tandem mass spectrometry.</p>
Kinase Assay	<p>Human CETP cDNA is amplified from a human liver cDNA library and the sequence is confirmed to be identical to the published sequence. The cDNA is subcloned into a pcDNA3.1 vector, under the control of CMV promoter. A stable line is established in CV1 cells in which the above-mentioned construct is used to express the recombinant human CETP. The medium contained the secreted recombinant CETP protein and the amount (19 ng/μL) is quantified by an ELISA kit. The medium is then aliquoted in 0.2% BSA and stored at -80°C. The stock CETP protein is diluted 150-fold in CETP buffer (10 mM Tris, 150 mM NaCl, and 2 mM EDTA) before use. The assay is set up in a 96-well plate. Each well received 97.5 μL diluted CETP protein (final concentration 7 nM) and 2.5 μL of compound stock. After a 30 min incubation at 37°C, 5 μL of substrate stock (the same stock used in the human plasma CETP assay), 0.16 μL of VLDL stock (2.5 mg/mL, Intracel) and 145 μL of CETP buffer are added, and the incubation is continued for another 4 h. Signal is read for the human plasma CETP assay[1].</p>
References	<p>[1]. Cao G, et al. Evacetrapib is a novel, potent, and selective inhibitor of cholesteryl ester transfer protein that elevates HDL cholesterol without inducing aldosterone or increasing blood pressure. J Lipid Res. 2011 Dec;52(12):2169-76.</p>