产品名称：雷马曲班
产品别名：**Ramatroban**

生物活性：

Description	Ramatroban is a selective thromboxane A_2 (TxA_2, IC_{50}=14 nM) antagonist, which also antagonizes CRTH2 (IC_{50}=113 nM) by inhibiting PGD_2binding.			
IC_{50} & Target	hTP	hDP2	hDP1	CYP 2C9
	14 nM (IC_{50})	311 nM (IC_{50})	33.4 μM (IC_{50})	15 μM (IC_{50})
In Vitro	Ramatroban is a potent human thromboxane receptor (hTP) antagonist with an IC_{50} of 18 nM in a human TP binding assay. Ramatroban inhibits prostaglandin D_2 receptor DP2 (CRTH2) with an IC_{50} of 113 nM in a human DP2 binding assay. Ramatroban also inhibits human CYP isoform CYP2C9 with an IC_{50} of 15 μM[1]. Ramatroban is a selective thromboxane-type prostanoid (TP) receptor antagonist. PGD_2-stimulated human eosinophil migration is shown to be mediated exclusively through activation of CRTH2, and surprisingly, these effects are completely inhibited by Ramatroban. Ramatroban is an antagonist for CRTH2, and inhibits PGD_2-induced migration of eosinophils via CRTH2 blockade. ^{3}H-labeled PGD_2 binds to a single site on CRTH2 transfectants with high affinity (K_D=6.3 nM, B_{max}=450 pM). Nonlabeled PGD_2 inhibits the binding of ^{3}H-labeled PGD_2 to CRTH2 transfectants in a concentration-dependent manner with an EC_{50} value of 2.7 nM. Ramatroban shows significant inhibitory effects on the binding of ^{3}H-labeled PGD_2 to CRTH2, albeit with much lower potency (IC_{50}=100 nM). Ramatroban also inhibits PGD_2-induced Ca^{2+} mobilization in CRTH2 transfectants to almost the same extent with an IC_{50} value of 30 nM. Ramatroban completely inhibits the PGD_2-induced migration of eosinophils in a concentration-dependent manner with an IC_{50} value of 170 nM[2].			
In Vivo	Ramatroban is an orally bioavailable small molecule antagonist of CRTH2. Systemic administration of Ramatroban (30 mg/kg) in $CRTH2^{+/+}$ mice produces the same effects as seen in CRTH2 deficiency. Ramatroban completely blocks LPS-induced decreases in social and object exploratory behavior ($p<0.01$). In addition, tumor-impaired social interaction and object exploratory behavior in $CRTH2^{+/+}$ mice are completely reversed by a single injection of Ramatroban, even when the tumor is enlarged [3].			
Solvent&Solubility	***In Vitro:*** **DMSO : 125 mg/mL** (**300.14 mM;** Need ultrasonic)			

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.4011 mL	12.0057 mL	24.0113 mL
	5 mM	0.4802 mL	2.4011 mL	4.8023 mL
	10 mM	0.2401 mL	1.2006 mL	2.4011 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: ≥ 2.08 mg/mL (4.99 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.99 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (4.99 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.99 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (4.99 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.99 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Stearns BA, et al. Novel tricyclic antagonists of the prostaglandin D_2 receptor DP2 with efficacy in a murine modelof allergic rhinitis. Bioorg Med Chem Lett. 2009 Aug 15;19(16):4647-51. [2]. Sugimoto H, et al. An orally bioavailable small molecule antagonist of CRTH2, ramatroban (BAY u3405), inhibits prostaglandin D_2-induced eosinophil migration in vitro. J Pharmacol Exp Ther. 2003 Apr;305(1):347-52. [3]. Haba R, et al. Central CRTH2, a second prostaglandin D_2 receptor, mediates emotional impairment in the lipopolysaccharide and tumor-induced sickness behavior model. J Neurosci. 2014 Feb 12;34(7):2514-23.

实验参考：

Cell Assay	Human eosinophils are purified and resuspended in migration buffer (20 mM HEPES, pH 7.6, 0.1% BSA, Hanks' solution) at a density of 6 ×10^6 cells/mL. Fifty microliters of the cell suspension (3×10^5 cells/well) is then dispensed into the upper chamber of a 96-well type chemotaxis chamber (pore diameter=5 μm), and 30 μL of ligand solution is added to the lower chamber. Cells are preincubated with various concentrations of Ramatroban (0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM and 10 μM) or BWA868C at 37°C for 10 min. The migration assays are performed in a humidified incubator at 37°C, 5% CO_2 for 2 h. The number of cells migrating into the lower chamber is counted [2].
Animal Administration	Mice[3] Five micrograms of LPS (closed columns) or saline (open columns) are intraperitoneally injected into CRTH2$^{+/+}$mice. CRTH2$^{+/+}$ mice are pretreated intraperitoneally for 1 h with 30 mg/kg Ramatroban.
Kinase Assay	CRTH2 transfectants are resuspended in binding buffer (50 mM Tris-HCl, pH 7.4, 40 mM $MgCl_2$, 0.1% BSA, 0.1% NaN_3). Cell suspension (2×10^5 cells), ^{3}H-labeled PGD_2, and various concentrations of Ramatroban (0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM and 10 μM) are then mixed in a 96-well U-bottomed polypropylene plate and incubated in a final volume of 100 μL for 60 min at

	room temperature. After incubation, the cell suspension is transferred to a filtration plate and washed three times with binding buffer. Scintillant is added to the filtration plate, and radioactivity remaining on the filter is measured by a scintillation counter. Nonspecific binding is determined by incubating the cell suspension and ^{3}H-labeled PGD_2 in the presence of 1 μM unlabeled PGD_2 [2].
References	[1]. Stearns BA, et al. Novel tricyclic antagonists of the prostaglandin D_2 receptor DP2 with efficacy in a murine modelof allergic rhinitis. Bioorg Med Chem Lett. 2009 Aug 15;19(16):4647-51. [2]. Sugimoto H, et al. An orally bioavailable small molecule antagonist of CRTH2, ramatroban (BAY u3405), inhibits prostaglandin D_2-induced eosinophil migration in vitro. J Pharmacol Exp Ther. 2003 Apr;305(1):347-52. [3]. Haba R, et al. Central CRTH2, a second prostaglandin D_2 receptor, mediates emotional impairment in the lipopolysaccharide and tumor-induced sickness behavior model. J Neurosci. 2014 Feb 12;34(7):2514-23.