产品名称：RVX 208
产品别名：Apabetalone；阿帕他隆

生物活性：

Description	Apabetalone (RVX-208) is an inhibitor of BET transcriptional regulators with selectivity for the second bromodomain. The IC_{50}s are 87±10 μM and 0.51±0.041 μM for BD1 and BD2, respectively.
IC_{50} & Target	IC50: 510±41 nM (BD2), 87±10 μM (BD1)[1]
In Vitro	Apabetalone (RVX-208) competes with binding of an acetylated histone peptide to tandem BD1 BD2 protein constructs of the four BET proteins, with IC_{50}s between 0.5 and 1.8 μM. Apabetalone increases the production of ApoA-I in hepatocytes in vitro, which results in increased high density lipoprotein cholesterol (HDL-C). Apabetalone selectively binds to bromodomains of the BET (Bromodomain and Extra Terminal) family, competing for a site bound by the endogenous ligand, acetylated lysine, and that this accounts for its pharmacological activity. Apabetalone increases Apolipoprotein A-I (ApoA-I) production through an epigenetic mechanism and suggests that BET inhibition may be a promising new approach to the treatment of atherosclerosis. Apabetalone increases ApoA-I expression in liver cells[2].
In Vivo	In the atherosclerosis prophylactic treatment study design, mice are fed a Western diet concurrent with the treatment with 150 mg/kg/dose b.i.d. for 12 weeks. Mice are sacrificed at 12 weeks after treatment. There is a progressive increase in body weight in both the vehicle treated as well as the Apabetalone (RVX-208) treated groups. However, there is only an increase of 4 g (from 24 g to 28 g) body weight after 12 weeks on Western diet in the Apabetalone treated group whereas this increase is found to be 9 g (25 g-34 g) in the vehicle treated group. The significant decrease in body weight gain in Apabetalone treated mice is not due to decreased feed consumption, suggesting a positive attribute of the molecule. Plasma lipid measurements are done at 6 weeks and 12 weeks of treatment with either the vehicle or Apabetalone. Compared to the vehicle control animals, Apabetalone treated mice show significant increase (~200%) in the levels of HDL-C at 6 weeks of treatment, which is sustained until end of the study (12 weeks)[3].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 33 mg/mL (89.09 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6998 mL	13.4989 mL	26.9978 mL
	5 mM	0.5400 mL	2.6998 mL	5.3996 mL
	10 mM	0.2700 mL	1.3499 mL	2.6998 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 (6.75 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.75 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。
References	[1]. Picaud S, et al. RVX-208, an inhibitor of BET transcriptional regulators with selectivity for the second bromodomain. Proc Natl Acad Sci U S A. 2013 Dec 3;110(49):19754-9. [2]. McLure KG, et al. RVX-208, an inducer of ApoA-I in humans, is a BET bromodomain antagonist. PLoS One. 2013 Dec 31;8(12):e83190. [3]. Jahagirdar R, et al. A novel BET bromodomain inhibitor, RVX-208, shows reduction of atherosclerosis in hyperlipidemic ApoE deficient mice. Atherosclerosis. 2014 Sep;236(1):91-100.

实验参考：

Cell Assay	Huh7 cells are plated at 23,000/well in a 96 well plate in DMEM+10% FBS before allowing to grow overnight. Cells are treated with compounds for 48 h in 0.1% DMSO with or without 5 μM Actinomycin D. U937 cells are differentiated for 3 days in 60 ng/mL PMA, 32,000 cells/well in 96-well format. Cells are then treated with compound in 0.1% DMSO in RPMI media+10% FBS, and after 1 h, lipopolysaccharide is added to the cells at 1 μg/mL for 3 hours[2].
Animal Administration	Mice[3] Seven to eight week old male ApoE-/- mice are used. Based on the body weight and lipid values, mice are divided into 2 groups (n=12): group 1, vehicle; and group 2, test agent, Apabetalone. Mice are then switched to Western diet (0.15% cholesterol and 42% calories from fat) and concurrently treated orally by gavage with either vehicle or the test agent, Apabetalone (150 mg/kg/dose b.i.d) for 12 weeks. After 6 week of treatment, an interim blood draw is done to monitor serum lipid levels. After 12 weeks of treatment mice are sacrificed to measure blood lipid parameters, aortic lesion, and liver and aortic RNA. Eight mice are used for enface (aortic plaque) analysis, 4 mice for tissue collection for mRNA and all 12 mice used for aortic sinus lesion area measurement.
References	[1]. Picaud S, et al. RVX-208, an inhibitor of BET transcriptional regulators with selectivity for the second bromodomain. Proc Natl Acad Sci U S A. 2013 Dec 3;110(49):19754-9. [2]. McLure KG, et al. RVX-208, an inducer of ApoA-I in humans, is a BET bromodomain antagonist. PLoS One. 2013 Dec 31;8(12):e83190. [3]. Jahagirdar R, et al. A novel BET bromodomain inhibitor, RVX-208, shows reduction of atherosclerosis in hyperlipidemic ApoE deficient mice. Atherosclerosis. 2014 Sep;236(1):91-100.