产品名称：Ozanimod
产品别名：奥扎莫德；RPC-1063

生物活性：

Description	Ozanimod is a potent and selective $S1P_1$ and $S1P_5$ receptor agonist with EC_{50}s of 410±160 pM and 11±4.3 nM in [^{35}S]-GTPγS binding, respectively.
IC_{50} & Target	EC50: 410±160 pM ($S1P_1$ receptor), 11±4.3 nM ($S1P_5$ receptor)[1]
In Vitro	Ozanimod (RPC1063) is a potent sphingosine-1-phosphate receptor-1 ($S1P_1$) and receptor-5 ($S1P_5$) agonist. The EC_{50} values are subnanomolar for $S1P_1$ receptors whether measuring inhibition of cAMP generation (160±60 pM) or [^{35}S]-GTPγS binding (410±160 pM). The EC_{50} value for $S1P_5$ receptor whether measuring inhibition [^{35}S]-GTPγS binding (11±4.3 nM). Ozanimod demonstrates agonist activity at the $S1P_5$ receptor [11±4.3 nM and 83% E_{max}(percentage of maximum stimulation)]. To determine whether Ozanimod induces sustained $S1P_1$ receptor internalization, $S1P_1$ receptor-HEK293T cells are incubated with different doses of Ozanimod in the presence of 10 μM cycloheximide to prevent translation of new $S1P_1$ receptor protein. Cells are analysed after 1 h treatment, or, after the 1 h treatment washed thoroughly to remove Ozanimod and incubated with 1 μM Cycloheximide for a further 24 h. After a 1 h treatment Ozanimod induces significant loss of $S1P_1$ receptor cell surface expression, similar in magnitude and potency to that seen with FTY720-P-treated cells. Following 1 h of treatment and a 24 h washout period, Ozanimod demonstrates a dose-dependent effect on $S1P_1$ receptor re-expression on the cell surface, with near complete and sustained loss of cell surface receptor expression at concentrations above 10 nM[1].
In Vivo	Ozanimod (RPC1063) is specific for $S1P_1$ and $S1P_5$ receptors, induces $S1P_1$ receptor internalization and induces a reversible reduction in circulating B and $CCR7^+$ T lymphocytes in vivo. Ozanimod shows high oral bioavailability and volume of distribution, and a circulatory half-life that supports once daily dosing. Oral Ozanimod reduces inflammation and disease parameters in all three autoimmune disease models[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 29 mg/mL (71.70 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4724 mL	12.3622 mL	24.7243 mL
5 mM	0.4945 mL	2.4724 mL	4.9449 mL
10 mM	0.2472 mL	1.2362 mL	2.4724 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 (6.18 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (6.18 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。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.18 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.18 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Scott FL, et al. Ozanimod (RPC1063) is a potent sphingosine-1-phosphate receptor-1 (S1P1) and receptor-5 (S1P5) agonist with autoimmune disease-modifying activity. Br J Pharmacol. 2016 Jun;173(11):1778-92.

实验参考：

Cell Assay	Representative histograms of transfected HEK293T cells expressing $S1P_1$ receptors incubated with vehicle control or 1 μM RPC1063. HEK293T cells are incubated with increasing doses of Ozanimod (0.01 nM, 0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM and 10 μM) for 1 h, or for 1 h followed by extensive washing to remove compound, then a 24 h recovery period and cell surface receptor expression is monitored[1].
Animal Administration	Mice[1] Female C57BL/6 mice (60 total, 10 weeks of age) are immunized with Myelin Oligodendrocyte Glycoproteins (MOG) $_{35-55}$ peptide with complete Freund's adjuvant on day 0, and pertussis toxin is administered 2 h and 24 h later. At the first instance of clinical symptoms of EAE (limp tail), mice are randomized into treatment groups (n=10 per group) and administered the test compound, p.o., once daily for 14 days. Mice that develop disease earlier than 9 days post-immunization are not enrolled, as these often develop fulminant disease that does not respond to therapy. Test compounds are 0.2 and 0.6 mg/kg Ozanimod, 3 mg/kg FTY720 or vehicle (5% DMSO, 5% Tween-20, 90% 0.1 N HCl). Animals are monitored daily for body weight and clinical symptoms and scored. At the end of the study, mice are anaesthetized via inhalation of isoflurane bubbled with oxygen at 10-20 kPa, blood drawn via cardiac puncture to exsanguination and analysed by a veterinary haemoanalyser.
References	[1]. Scott FL, et al. Ozanimod (RPC1063) is a potent sphingosine-1-phosphate receptor-1 (S1P1) and receptor-5 (S1P5) agonist with autoimmune disease-modifying activity. Br J Pharmacol. 2016 Jun;173(11):1778-92.