产品名称：Lomitapide
产品别名：洛美他派

生物活性：

Description	Lomitapide (AEGR-733; BMS-201038) is a potent inhibitor of microsomal triglyceride-transfer protein (MTP) with an IC_{50} of 8 nM in vitro.
IC_{50} & Target	IC50: 8 nM (MTP)[1]
In Vitro	Lomitapide is an oral microsomal triglyceride transfer protein (MTP) inhibitor indicated for the treatment of patients with HoFH, a rare form of hypercholesterolemia that can lead to premature atherosclerotic disease. Lomitapide undergoes hepatic metabolism via cytochrome P-450 (CYP) isoenzyme 3A4 and interacts with CYP3A4 substrates including atorvastatin and simvastatin[2].
In Vivo	The use of lomitapide alone or in combination with other lipid-lowering modalities reduces plasma concentrations of low density lipoprotein cholesterol (LDL-C) by a mean of more than 50%. Lomitapide is associated with significant gastrointestinal adverse effects and increases in hepatic fat levels. The bioavailability of the 50-mg lomitapide capsule is 7.1%. The mean half-life of lomitapide is 39.7 hours[2]. Single-dose administration of lomitapide is shown to reduce serum triglycerides by 35% and 47% at 0.3- and 1-mg/kg doses, respectively. Multiple-dose treatment with lomitapide also results in dose dependent decrease in triglycerides (71%–87%), nonesterified fattyacids(33%–40%), and LDL-C(26-29%)[3].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (144.15 mM)** **H2O : < 0.1 mg/mL (insoluble)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.4415 mL	7.2075 mL	14.4150 mL
5 mM	0.2883 mL	1.4415 mL	2.8830 mL
10 mM	0.1442 mL	0.7208 mL	1.4415 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 (3.60 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (3.60 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% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (3.60 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (3.60 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 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: ≥ 2.5 mg/mL (3.60 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.60 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]. Sulsky R, et al. 5-Carboxamido-1,3,2-dioxaphosphorinanes, potent inhibitors of MTP. Bioorg Med Chem Lett. 2004 Oct 18;14(20):5067-70. [2]. Davis KA. et al. Lomitapide: A novel agent for the treatment of homozygous familial hypercholesterolemia. Am J Health Syst Pharm. 2014 Jun 15;71(12):1001-8. [3]. Dhote V, et al. Inhibition of microsomal triglyceride transfer protein improves insulin sensitivity and reduces atherogenic risk in Zucker fatty rats. Clin Exp Pharmacol Physiol. 2011 May;38(5):338-44.

实验参考：

Animal Administration	Rats: BMS-201038 is formulated in 0.1% hydroxyl ethyl cellulose and 0.5% Tween 80 in deionized water. Rats in the control group are administered vehicle (2 mL/kg) p.o. Fasted rats are administered 0.3 and 1 mg/kg, p.o., BMS-201038, followed 1 h later by 250 mg/kg, i.v., Triton WR1339. Blood samples are obtained from rats up to 240 min after Triton WR1339 injection to estimate serum triglyceride concentrations. For evaluation of post-prandial lipaemia, fasted rats are administered 0.3 and 1 mg/kg, p.o., BMS-201038, followed 1 h later by a corn oil bolus (6 mL/kg) by oral gavage. Blood samples are again collected up to 1440 min after corn oil administration for the estimation of serum triglyceride concentrations[3].
References	[1]. Sulsky R, et al. 5-Carboxamido-1,3,2-dioxaphosphorinanes, potent inhibitors of MTP. Bioorg Med Chem Lett. 2004 Oct 18;14(20):5067-70. [2]. Davis KA. et al. Lomitapide: A novel agent for the treatment of homozygous familial hypercholesterolemia. Am J Health Syst Pharm. 2014 Jun 15;71(12):1001-8. [3]. Dhote V, et al. Inhibition of microsomal triglyceride transfer protein improves insulin sensitivity and reduces atherogenic risk in Zucker fatty rats. Clin Exp Pharmacol Physiol. 2011 May;38(5):338-44.