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产品名称：BMS-927711
产品别名：Rimegepant

生物活性：

Description	Rimegepant (BMS-927711) is a highly potent, oral calcitonin gene-related peptide (CGRP) receptor antagonist with a Ki value of 0.027 nM.
IC_{50} & Target	Ki: 0.027 nM (CGRP receptor)[1] IC50: 0.14 nM (CGRP receptor)[1]
In Vitro	Rimegepant (BMS-927711) is a full, competitive CGRP receptor antagonist with IC_{50} of 0.14±0.01 nM[1].
In Vivo	Rimegepant (BMS-927711) has good oral bioavailability in rat and cynomolgus monkey, attractive overall preclinical properties, and shows dose-dependent activity in a primate model of CGRP-induced facial blood flow[1]. The ratios of the mean AUC (0-24 h) values for Rimegepant (BMS-927711) (60, 100, and 300 mg/kg) in the DBS matrix, compare with plasma, are 0.5-0.6 across all doses in rats. Results from this study suggest a strong correlation of Rimegepant concentrations between rat plasma and rat blood (DBS)[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 10 mg/mL** (**18.71 mM;** Need ultrasonic and warming) **Ethanol : 10 mg/mL** (**18.71 mM;** Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8707 mL	9.3535 mL	18.7070 mL
	5 mM	0.3741 mL	1.8707 mL	3.7414 mL
	10 mM	0.1871 mL	0.9353 mL	1.8707 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；该产品在溶液状态不稳定，建议您现用现配，即刻使用。

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% EtOH →90% PEG300

Solubility: ≥ 1 mg/mL (1.87 mM); Clear solution

References

[1]. Luo G, et al. Discovery of (5S,6S,9R)-5-amino-6-(2,3-difluorophenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-yl 4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)piperidine-1-carboxylate (BMS-927711): an oral calcitonin gene-related peptide (CGRP) antagonist in clinical trials for treating migraine. J Med Chem. 2012 Dec 13;55(23):10644-51.

[2]. Zheng N, et al. Improved liquid-liquid extraction with inter-well volume replacement dilution workflow and its application to quantify BMS-927711 in rat dried blood spots by UHPLC-MS/MS. J Pharm Biomed

	Anal. 2014 Feb;89:240-50.

实验参考：

Animal Administration	Rats[2] Rats are treated with drug-free vehicle (control) or Rimegepant (BMS-927711) in vehicle at 60, 100, and 300 mg/kg once daily via oral gavage. There are 6 rats in each treatment group. For each treatment group, blood is collected at 1, 6, and 24 h from first three rats, and at 3 and 8 h from the second three rats on Day 1 and Day 14 from the tail vein following daily oral dosing of Rimegepant (BMS-927711) for two weeks. The mean hematocrits in the blood are 50.2±1.8%, 49.8±2.2%, 46.4±5.2% corresponding to the animal groups of 60, 100, and 300 mg/kg doses, respectively. For DBS evaluation, four 15 μL blood samples are spotted onto DBS cards (4 spots per card), dried at room temperature for at least 2 h, and each card is packaged separately in a ziplock bag with desiccant prior to shipment. The remaining blood in each sample tube is processed to plasma within 1 h of collection and stored at -70°C until analysis. Plasma samples are shipped on dry ice, and DBS cards are shipped at ambient temperature. Rimegepant (BMS-927711) concentrations in rat plasma are analyzed. Rimegepant in rat DBS is analyzed using the DBS method. The toxicokinetic (TK) parameters are calculated from blood concentration and time data using non-compartmental methods using Kinetica.
References	[1]. Luo G, et al. Discovery of (5S,6S,9R)-5-amino-6-(2,3-difluorophenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-yl 4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)piperidine-1-carboxylate (BMS-927711): an oral calcitonin gene-related peptide (CGRP) antagonist in clinical trials for treating migraine. J Med Chem. 2012 Dec 13;55(23):10644-51. [2]. Zheng N, et al. Improved liquid-liquid extraction with inter-well volume replacement dilution workflow and its application to quantify BMS-927711 in rat dried blood spots by UHPLC-MS/MS. J Pharm Biomed Anal. 2014 Feb;89:240-50.