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产品名称：SLV-319
产品别名：(±)-Ibipinabant；(±)-SLV319; (±)-BMS6462

生物活性：

Description	(±)-Ibipinabant ((±)-SLV319) is the racemate of SLV319. (±)-Ibipinabant ((±)-SLV319) is a potent and selective cannabinoid-1 (CB-1) receptor antagonist with an IC_{50} of 22 nM.
IC_{50} & Target	IC50: 22 nM (CB-1)[1]; Ki: 7.8 nM (CB-1)[2]
In Vitro	Cannabinoid receptor 1 (CB1R) antagonists appear to be promising drugs for the treatment of obesity, however, serious side effects have hampered their clinical application. Ibipinabant is a new, potent [Ki (CB1)=7.8 nM] and selective [Ki (CB2)=7.943 nM] CB1 antagonist [pA2 for arachidonic acid release in CHO cells=9.9] with in vitro pharmacological characteristics similar to rimonabant including inverse agonism and brain penetrance[3].
In Vivo	(±)-Ibipinabant ((±)-SLV319) (3 mg/kg) reduces unfasted glucose to a significantly greater degree than rimonabant at the same dose on days 17, 28 and 38. Chronic treatment with (±)-Ibipinabant ((±)-SLV319) significantly attenuates the progression of diabetes in ZDF rats, blunting the increase in blood glucose and HbA1c over time. Ibipinabant also reduces the hyperinsulinemia apparent at 6-8 weeks of age and attenuates the dramatic reduction in insulin levels observed 1-2 weeks later[3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 31 mg/mL (63.60 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0517 mL	10.2585 mL	20.5170 mL
	5 mM	0.4103 mL	2.0517 mL	4.1034 mL
	10 mM	0.2052 mL	1.0259 mL	2.0517 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 (stored under nitrogen)。-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 (5.13 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.13 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 (5.13 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.13 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]. Chorvat RJ, et al. JD-5006 and JD-5037: peripherally restricted (PR) cannabinoid-1 receptor blockers related to SLV-319 (Ibipinabant) as metabolic disorder therapeutics devoid of CNS liabilities. Bioorg Med Chem Lett. 2012 Oct 1;22(19):6173-80. [2]. Lange JH, et al. Synthesis, biological properties, and molecular modeling investigations of novel 3,4-diarylpyrazolines as potent and selective CB(1) cannabinoid receptor antagonists. J Med Chem. 2004 Jan 29;47(3):627-43. [3]. Rohrbach K, et al. Ibipinabant attenuates β-cell loss in male Zucker diabetic fatty rats independently of its effects on body weight. Diabetes Obes Metab. 2012 Jun;14(6):555-64.

实验参考：

Animal Administration	Rats: SLV319, rimonabant and rosiglitazone are suspended in a 10% dimethylacetamide, 10% cremophor, 10% ethanol and 70% water vehicle. Drugs are administered by oral gavage in a volume of 2 mL/kg body weight at 09:00 hours every day. Treatment groups are as follows: (i) Vehicle: ad libitum access to food (vehicle), (ii) Vehicle: restricted access to food (20% less than average food intake of ad libitum vehicle-treated group for the first 3 days of the study, then 10% less than the average food intake of the ad libitum vehicle-treated group for the remainder of the study) (restricted), (iii) Rosiglitazone (4 mg/kg), (iv) Rimonabant (3 mg/kg) (RIM 3 mg/kg), (v) Rimonabant (10 mg/kg) (RIM 10 mg/kg), (vi) (±)-Ibipinabant ((±)-SLV319) (3 mg/kg) (IBI 3 mg/kg) and (vii) Ibipinabant (10 mg/kg) (IBI 10 mg/kg). Rosiglitazone is used as a positive control for its ability to delay β-cell decline, and rimonabant is used as a positive control for CB1 antagonism[3].
References	[1]. Chorvat RJ, et al. JD-5006 and JD-5037: peripherally restricted (PR) cannabinoid-1 receptor blockers related to SLV-319 (Ibipinabant) as metabolic disorder therapeutics devoid of CNS liabilities. Bioorg Med Chem Lett. 2012 Oct 1;22(19):6173-80. [2]. Lange JH, et al. Synthesis, biological properties, and molecular modeling investigations of novel 3,4-diarylpyrazolines as potent and selective CB(1) cannabinoid receptor antagonists. J Med Chem. 2004 Jan 29;47(3):627-43. [3]. Rohrbach K, et al. Ibipinabant attenuates β-cell loss in male Zucker diabetic fatty rats independently of its effects on body weight. Diabetes Obes Metab. 2012 Jun;14(6):555-64.