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产品名称：Rislenemdaz
产品别名：MK-0657; CERC-301

生物活性：

Description	Rislenemdaz (CERC-301) is an orally bioavailable and selective N-methyl-D-aspartate (NMDA) receptor subunit 2B (GluN2B) antagonist with K_i and IC_{50} of 8.1 nM and 3.6 nM, respectively.
IC_{50} & Target	IC50: 3.6 nM (GluN2B)[1] Ki: 8.1 nM (GluN2B)[1]
In Vitro	Rislenemdaz (CERC-301) inhibits calcium influx into agonist-stimulating NMDA-GluN1a/GluN2B L(tk-) cells with an IC50 of 3.6 nM. Rislenemdaz exhibits at least 1000× selectivity for the GluN2B receptor versus all targets tested, including the hERG potassium channel. Rislenemdaz also exhibits minimal activity against sigma-type receptors at 10 uM[1].
In Vivo	Rislenemdaz (CERC-301) (1, 3, 10, and 30 mg/kg) significantly decreases immobility frequency (P<0.001) and significantly increases swimming behavior (P<0.01 for 1, 3, and 30 mg/kg; P<0.05 for 10 mg/kg) compare to the vehicle control. Rislenemdaz plasma levels are approximately 15, 120, 390, 1420, 4700, and 14,110 nM (0.015, 0.120, 0.390, 1.42, 4.7, and 14.11 uM) at the time of sampling, corresponding to approximately 5, 29, 56, 83, 94, and 98% RO, respectively, in rats. The ED_{50} for increaing in frequency of swimming and decreasing in immobility are ~0.3 and 0.7 mg/kg, respectively, corresponding to RO of ~30 and 50%. Rislenemdaz (1, 3, 10, and 30 mg/kg) significantly increases total distance traveling (P<0.01 for 1 mg/kg; P<0.001 for 3, 10, and 30 mg/kg) compare to vehicle control over the 60 min test[1].
Solvent&Solubility	***In Vitro:*** **DMSO： 100 mg/mL (279.01 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7901 mL	13.9505 mL	27.9010 mL
	5 mM	0.5580 mL	2.7901 mL	5.5802 mL
	10 mM	0.2790 mL	1.3951 mL	2.7901 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: ≥ 0.83 mg/mL (2.32 mM); Clear solution

此方案可获得 ≥ 0.83 mg/mL (2.32 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 8.3 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: ≥ 0.83 mg/mL (2.32 mM); Clear solution 此方案可获得 ≥ 0.83 mg/mL (2.32 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 8.3 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: ≥ 0.83 mg/mL (2.32 mM); Clear solution 此方案可获得 ≥ 0.83 mg/mL (2.32 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 8.3 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Rachel Garner, et al. Preclinical pharmacology and pharmacokinetics of CERC‐301, a GluN2B‐selective N‐methyl‐D‐aspartate receptor antagonist. Pharmacol Res Perspect. 2015 Dec; 3(6): e00198.

实验参考：

Cell Assay	Rat, dog, rhesus monkey, and human plasma samples (3 mL, N=3) are incubated with 2 and 20 uM [^{14}C] Rislenemdaz at 37°C for 30 min in a shaking water bath. Following incubation, standard ultracentrifugation methodology is used to determine the percentage of drug unbind[1].
Animal Administration	Four groups of 24 rats (12/sex) are given single doses of vehicle (0.5% methylcellulose [MC] and 0.02% sodium lauryl sulfate [SLS] in deionized water) or Rislenemdaz at 10, 30 or 100 mg/kg by oral gavage at a dose volume of 10 mL/kg. Three additional groups of rats (four males and three females per group) are orally dosed in the same manner with Rislenemdaz, and 24h serial blood samples are obtained and analyzed for Rislenemdaz plasma concentrations and evaluated for systemic exposure. Young, adult, male rats are randomly assigned across the treatment groups and are administered vehicle (0.5% MC/0.02% SLS), the reference compound desipramine (20 mg/kg; a tricyclic antidepressant) dissolving in sterile water, or Rislenemdaz (0.1, 0.3, 1, 3, 10, and 30 mg/kg) suspending in 0.5% MC/0.02% SLS, twice on Day 1 (after habituation; ~24 h prior to test, and prior to dark cycle) and once on Day 2 (30 min pretest for desipramine and 45 min pretest for Rislenemdaz and vehicle)[1].
References	[1]. Rachel Garner, et al. Preclinical pharmacology and pharmacokinetics of CERC‐301, a GluN2B‐selective N‐methyl‐D‐aspartate receptor antagonist. Pharmacol Res Perspect. 2015 Dec; 3(6): e00198.