产品名称：Latrepirdine
产品别名：Latrepirdine dihydrochloride；Dimebolin dihydrochloride

生物活性：

Description	Latrepirdine dihydrochloride is a neuroactive compound with antagonist activity at histaminergic, α-adrenergic, and serotonergic receptors. Latrepirdine stimulates amyloid precursor protein (APP) catabolism and amyloid-β (Aβ) secretion.
IC_{50} & Target	Amyloid-β (Aβ), Histaminergic receptor, α-adrenergic receptor, Serotonergic receptor[1]
In Vitro	Latrepirdine has been reported to possess several properties that are potentially relevant to the treatment of neurodegenerative diseases: (1) protection of cultured cells from the cytotoxicity of amyloid-β (Aβ) peptide; (2) stabilization of mitochondrial function and calcium homeostasis; (3) modulation of Aβ release from cultured cells, isolated intact nerve terminals, and from hippocampal neurons in living mouse brain; and (4) promotion of neurogenesis in the murine hippocampus. Treatment of cultured mammalian cells with Latrepirdine leads to enhanced mTOR- and Atg5-dependent autophagy. Latrepirdine modulates Atg5-dependent autophagic activity in a dose-dependent manner and via the mTOR-signaling pathway. HeLa cells stably expressing LC3 fused are treated with EGFP (eGFP-LC3) for 3 or 6 hours in the absence or presence of 50 μM Latrepirdine. Treatment with Latrepirdine for 3 or 6 hours markedly enhances the number of eGFP-LC3 punctae, indicating that Latrepirdine induces formation of autophagosomes. Next, mouse N2a neuroblastoma cells are treated in the absence (vehicle) or presence of 5 nM, 500 nM or 50 μM Latrepirdine for 3 or 6 hours in order to determine the effects of acute drug treatment on the regulation of autophagy. A significant and dose-dependent increase is observed in LC3-II levels in N2a cells following 3- or 6-hour treatment with either 500 nM or 50 μM Latrepirdine. A significant decrease of p-mTOR and p-S6K from N2a cells treated with 50 μM Latrepirdine for 3 hours is observed, whereas the total mTOR and p70S6K levels remain relatively constant[1].
In Vivo	Latrepirdine treatment of TgCRND8 transgenic mice is associated with improved learning behavior and with a reduction in accumulation of Aβ42 and α-synuclein. Male, 90-day-old TgCRND8 mice or their wild-type littermates (nTg) receive 31 consecutive once daily i.p. injections of either 3.5 mg/kg Latrepirdine or 0.9% saline (vehicle). At the culmination of treatment, mice are tested for cued and contextual fear conditioning using a paradigm that has been widely accepted for evaluating learning and memory deficits in APP transgenic mice. A significant increase in cued memory only among Latrepirdine-versus vehicle-treated TgCRND8 mice (p=0.01) is observed. A weak, non-significant trend toward an improvement in contextual memory among Latrepirdine-versus vehicle-treated mice (p=0.099) is also observed[1].

In Vitro:

DMSO : 6.4 mg/mL (**16.31 mM;** Need warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.5486 mL	12.7431 mL	25.4861 mL
	5 mM	0.5097 mL	2.5486 mL	5.0972 mL
	10 mM	0.2549 mL	1.2743 mL	2.5486 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:

Solvent&Solubility	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: ≥ 0.5 mg/mL (1.27 mM); Clear solution 此方案可获得 ≥ 0.5 mg/mL (1.27 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 5.0 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: ≥ 0.5 mg/mL (1.27 mM); Clear solution 此方案可获得 ≥ 0.5 mg/mL (1.27 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 5.0 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: ≥ 0.5 mg/mL (1.27 mM); Clear solution 此方案可获得 ≥ 0.5 mg/mL (1.27 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 5.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Steele JW, et al. Latrepirdine improves cognition and arrests progression of neuropathology in an Alzheimer's mouse model. Mol Psychiatry. 2013 Aug;18(8):889-97.

实验参考：

Cell Assay	N2a cells, stable human cervical carcinoma (HeLa) cells expressing EGFP-LC3, and mouse embryonic fibroblasts (MEFs) derived from wildtype mice or ATG5$^{-/-}$ mice are maintained in “growth medium” (high glucose Dulbecco's modified Eagle's medium supplemented with 10% FBS and 100 units/mL Penicillin/Streptomycin) at 37°C, 5% CO_2. N2a cells stably transfected with APPK670N, M671L are maintained in growth medium supplemented with 0.2 mg/mL G418. Cells are washed 1× with ice cold PBS (pH 7.4) then incubated with either Latrepirdine (5 nM, 500 nM or 50 μM) or vehicle (growth medium). Following 3-, 6-, or 24-hour of treatment, cells are washed 1x with ice cold PBS, and collected in lysis buffer (50 mM Tris-HCl, 150 mM NaCl, 1 mM Pepstatin, 1 mM PMSF, 1% Triton X-100, EDTA-free mini-complete protease inhibitor cocktail tablet) then centrifuged (14,000 RPM) for 15 minutes at 4°C. For time-course experiments, cells are washed 2× with ice-cold PBS (pH 7.4) and incubated for the indicated time in serum-free DMEM containing 50 μg/mL CHX or 50 μg/mL Cycloheximide (CHX)+50 μg/mL Chloroquine (CQ). Baseline (T_0) samples are collected immediately prior to treatment[1]
	Mice[1] Male 53-55-day-old TgCRND8 mice (N=25) are randomly distributed into either of the two treatment groups: Latrepirdine (n=13 TgCRND8) or vehicle (n=12 TgCRND8). Animals receive 21 consecutive once daily intraperitoneal injections of either 3.5 mg/kg Latrepirdine or 0.9% saline (vehicle). 90-day-old male TgCRND8 mice (N=28) or their wild-type littermates (N=56) are randomly

Animal Administration	distributed into either of two treatment groups: Latrepirdine (n=13 TgCRND8; n=21 nTg) or vehicle (n=15 TgCRND8; n=25 nTg). Following treatment, animals are sacrificed and transcardially perfused with ice-cold PBS (pH 7.4). Male 90-day-old (n=5 per genotype) or 120-day-old (n=6 per genotype) TgCRND8 mice or their non-transgenic littermates are sacrificed and transcardially perfused with ice-cold PBS (pH 7.4). One hemisphere from each mouse is post-fixed in 4% paraformaldeyhde in PBS (pH 7.4) for histological analysis and the other hemisphere is dissected and snap-frozen for biochemical analysis.
References	[1]. Steele JW, et al. Latrepirdine improves cognition and arrests progression of neuropathology in an Alzheimer's mouse model. Mol Psychiatry. 2013 Aug;18(8):889-97.