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产品名称：ADX88178
产品别名：ADX88178

生物活性：

Description	ADX88178 is a potent metabotropic glutamate receptor 4 positive allosteric modulator (mGluR4 PAM) with an $EC_{50}$of 4 nM for human mGluR4.
IC_{50} & Target	EC50: 4 nM (human mGluR4)[1]
In Vitro	ADX88178 is developed as a potent and selective mGluR4 positive allosteric modulator. ADX88178 is used as a novel radioligand for imaging of metabotropic glutamate receptor subtype 4 (mGluR4). ADX88178 potentiates glutamate-mediated activation of human mGluR4 with EC50 values of 4 nM without significant effects on other mGluRs (EC50 > 30 μM)[1]. ADX88178 is novel potent, selective, and brain-penetrant positive allosteric modulator of the mGlu4. Microglia are pretreated with 1, 10 or 100 nM ADX88178 or 100 nM LAP4 for 30 min followed by LPS treatment for 24 h prior to collecting culture supernatant for ELISA measurement of TNFα levels. The pre-treatment with ADX88178 and LAP4 both significantly attenuate LPS-induced TNFα levels. As little as 1 nM of ADX88178 is sufficient to inhibit TNFα, and is as effective at concentrations of 10 and 100 nM[2].
In Vivo	In mice, ADX88178 (1-30 mg/kg p.o.) dose-dependently increases the number of open-arm entries. Specifically, at 3, 10, and 30 mg/kg ADX88178, there are 5-, 7-, and almost 13-fold increases in the number of open-arm entries, respectively, when compared with the vehicle-treated controls. Also, ADX88178 dose-dependently increases the time spent in the open arms. Specifically, at 3, 10, and 30 mg/kgADX88178, there are 8-, 12-, and 24-fold increases in the time spent in the open arms when compared with the vehicle-treated controls. In rats, ADX88178 (10-100 mg/kg p.o.) dose-dependently increases the number of open-arm entries in the rat EPM test. Specifically, at 10, 30, and 100 mg/kg ADX88178, there are 5-, 8-, and more than 10-fold increases in the number of open-arm entries, respectively, when compared with the vehicle-treated controls. Also, ADX88178 dose-dependently increases the time spent in the open arms. Specifically, at 10, 30, and 100 mg/kg ADX88178, there are 7.5-, 11-, and 13-fold increases in time spent in the open arms when compared with the vehicle-treated controls[3].

In Vitro:

DMSO : 16.67 mg/mL (61.21 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.6720 mL	18.3601 mL	36.7202 mL
	5 mM	0.7344 mL	3.6720 mL	7.3440 mL
	10 mM	0.3672 mL	1.8360 mL	3.6720 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

Solvent&Solubility	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: ≥ 1.67 mg/mL (6.13 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (6.13 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 16.699999 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。
References	[1]. Fujinaga M, et al. Radiosynthesis and evaluation of 5-methyl-N-(4-[(11)C]methylpyrimidin-2-yl)-4-(1H-pyrazol-4-yl)thiazol-2-amine ([(11)C]ADX88178) as a novel radioligand for imaging of metabotropic glutamate receptor subtype 4 (mGluR4). Bioorg Med Chem Lett. 2016 Jan 15;26(2):370-4. [2]. Ponnazhagan R, et al. The Metabotropic Glutamate Receptor 4 Positive Allosteric Modulator ADX88178 Inhibits Inflammatory Responses in Primary Microglia. J Neuroimmune Pharmacol. 2016 Jun;11(2):231-7. [3]. Kalinichev M, et al. Characterization of the novel positive allosteric modulator of the metabotropic glutamate receptor 4 ADX88178 in rodent models of neuropsychiatric disorders. J Pharmacol Exp Ther. 2014 Sep;350(3):495-505.

实验参考：

Cell Assay	After adhesion to the chamber slides, microglia from WT and mGlu4 KO microglia pre-treated with 1 nM, 10 nM, 100 nM ADX88178, or 100 nM L-AP4. Each treatment is performed in quadruplicate. Thirty minutes after treatment with ADX88178 or L-AP4, 100 ng/mL LPS is added to the cultures and the cells are incubated at 37 °C for an additional 24 h. At the end of the 24 h treatment period, media is collected and analyzed for TNFα, and the cells are for iNOS and MHC II expression by immunocytochemistry[2].
Animal Administration	Mice and Rats[3] Male mice (n=8-10/group) are treated orally (p.o.) via gavage with vehicle [1% carboxymethyl cellulose (CMC)], ADX88178 (1, 3, 10 and 30 mg/kg) or Diazepam (1.5 mg/kg). Male rats (n=10/group) are treated p.o. with vehicle (1% CMC), ADX88178 (10, 30, and 100 mg/kg), or Diazepam (3 mg/kg). After 60 minutes, animals are individually placed in the center of the maze (facing one of the closed arms) and left to explore for 5 minutes. A terminal blood sample is collected from all ADX88178-treated animals at the end of the experiment, and plasma is analyzed for the pharmacokinetic studies. The number of open-arm and closed-arm entries, as well as the time (seconds) spent in the open arms of the maze, is analyzed by one-way analysis of variance followed by Dunnett's test.
References	[1]. Fujinaga M, et al. Radiosynthesis and evaluation of 5-methyl-N-(4-[(11)C]methylpyrimidin-2-yl)-4-(1H-pyrazol-4-yl)thiazol-2-amine ([(11)C]ADX88178) as a novel radioligand for imaging of metabotropic glutamate receptor subtype 4 (mGluR4). Bioorg Med Chem Lett. 2016 Jan 15;26(2):370-4. [2]. Ponnazhagan R, et al. The Metabotropic Glutamate Receptor 4 Positive Allosteric Modulator

	ADX88178 Inhibits Inflammatory Responses in Primary Microglia. J Neuroimmune Pharmacol. 2016 Jun;11(2):231-7. [3]. Kalinichev M, et al. Characterization of the novel positive allosteric modulator of the metabotropic glutamate receptor 4 ADX88178 in rodent models of neuropsychiatric disorders. J Pharmacol Exp Ther. 2014 Sep;350(3):495-505.