

Product Data Sheet

Product Name: ADX88178

Cat. No.: GC30793

Chemical Properties

Cas. No. 1235318-89-4

SMILES CC1=C(C2=CN=C2)N=C(NC3=NC=CC(C)=N3)S1

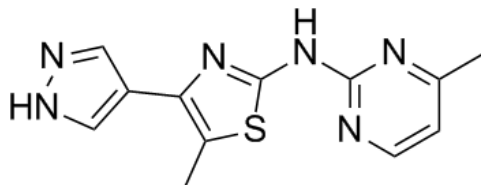
Formula $C_{12}H_{12}N_6S$ M.Wt 272.33

Solubility DMSO : ≥ 50 mg/mL (183.60 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Cell experiment: 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 TNF α , and the cells are for iNOS and MHC II expression by immunocytochemistry[2].

Animal experiment: 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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

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.

Background

ADX88178 is a potent positive allosteric modulator for metabotropic glutamate receptor 4 (mGluR4) with EC₅₀ of 4 nM for human mGluR4.

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 μ M)[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 TNF α levels. The pre-treatment with ADX88178 and LAP4 both significantly attenuate LPS-induced TNF α levels. As little as 1 nM of ADX88178 is sufficient to inhibit TNF α , and is as effective at concentrations of 10 and 100 nM[2].

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/kg ADX88178, 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

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

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].

[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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA