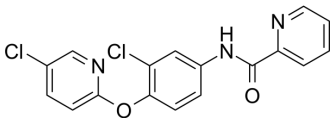
VU0422288

Cat. No.:	HY-110190
CAS No.:	1630936-95-6
Molecular Formula:	$C_{17}H_{11}Cl_2N_3O_2$
Molecular Weight:	360.19
Target:	mGluR
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (69.41 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7763 mL	13.8816 mL	27.7631 mL
	5 mM	0.5553 mL	2.7763 mL	5.5526 mL
	10 mM	0.2776 mL	1.3882 mL	2.7763 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

VU0422288 (ML396) is a positive allosteric modulator of group III mGluRs. VU0422288 inhibits mGluRs with EC_{50}s of 125 nM, 146 nM, and 108 nM for mGluR4, mGluR7, and mGluR8, respectively in calcium mobilization assays. VU0422288 reverses deficits in contextual fear memory, social recognition, and apneas in Rett syndrome (RTT) model mice[1][2].

IC_{50} & Target			
	mGluR4 108 nM (EC50)	mGluR7 146 nM (EC50)	mGluR8 128 nM (EC50)

In Vitro

VU0422288 (1 μM; 5 min) enhances 30 μM LSP4-2022-induced reductions in the field excitatory postsynaptic potentials (fEPSPs) slope on Coronal slices containing the hippocampus[1].

VU0422288 (1 μM; 10 min) can not alter the fEPSP slopes alone, indicating that mGlu7 is not tonically active in $Mecp2^{-/y}$ slices under stimulation conditions[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	VU0422288 (30 mg/kg; i.p.; once daily for 17 days) rescues synaptic plasticity defects and learning and memory phenotypes, reduces the number of apneas in $Mecp2^{+/-}$ mice, while VU0422288 has no effect in $Mecp2^{+/+}$ animals[2]. VU0422288 (10 mg/kg; i.p.; single dose) exhibis a plasma/brain partitioning coefficient of 1.67 in adult male Sprague-Dawley rats, with predicted unbound brain concentration of about 40 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Gogliotti RG, et al. mGlu7 potentiation rescues cognitive, social, and respiratory phenotypes in a mouse model of Rett syndrome. Sci Transl Med. 2017 Aug 16;9(403):eaai7459.

[2]. Jalan-Sakrikar N, et al. Identification of positive allosteric modulators VU0155094 (ML397) and VU0422288 (ML396) reveals new insights into the biology of metabotropic glutamate receptor 7. ACS Chem Neurosci. 2014 Dec 17;5(12):1221-37.

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