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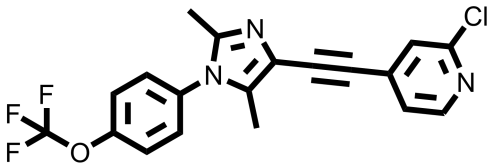
mGlu5 Antagonist – CTEP

Chemical Name: 2-chloro-4-((2,5-dimethyl-1-(4-(trifluoromethoxy)phenyl)-1H-imidazol-4-yl)ethynyl)pyridine



Molecular Weight:	391.77
Formula:	$C_{19}H_{13}ClF_3N_3O$
Purity:	≥ 98%
CAS#:	871362-31-1
Solubility:	DMSO up to 100 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

CTEP is a highly potent, selective and orally bioavailable allosteric antagonist of mGlu5 receptor with an IC_{50} of 2.2 nM. It shows >1000-fold selectivity against 103 targets, including all known mGlu receptors. CTEP can penetrate the brain with a brain/plasma ratio of 2.6. CTEP is active in the stress-induced hyperthermia procedure in mice and the Vogel conflict drinking test in rats with minimal effective doses of 0.1 and 0.3 mg/kg, respectively, reflecting a 30- to 100-fold higher in vivo potency compared with 2-methyl-6-(phenylethynyl)pyridine (MPEP) and fenobam. CTEP is the first reported mGlu5 inhibitor with both long half-life of approximately 18 h and high oral bioavailability allowing chronic treatment with continuous receptor blockade with one dose every 48 h in adult and newborn animals. Acute CTEP treatment corrects elevated hippocampal long-term depression, protein synthesis, and audiogenic seizures. Chronic treatment that inhibits mGlu5 within a receptor occupancy range of 81% ± 4% rescues cognitive deficits, auditory hypersensitivity, aberrant dendritic spine density, overactive ERK and mTOR signaling, and partially corrects macroorchidism. By enabling long-term treatment through a wide age range, CTEP allows the exploration of the full therapeutic potential of mGlu5 inhibitors for indications requiring chronic receptor inhibition.

How to Use:

In vitro: CTEP was used at 0.03-0.1 μM final concentration in vitro and in cellular assays.

In vivo: CTEP was orally dosed to mice at single 0.1-1.0 mg/kg, or with a dose of 2 mg/kg orally every 48 h for 2 months. CTEP was orally dose at 2 mg/kg BID achieves uninterrupted mGlu5 occupancy per 48 hours in mice.

Reference:

1. Lindemann L, et al. CTEP: a novel, potent, long-acting, and orally bioavailable metabotropic glutamate receptor 5 inhibitor. (2011) J Pharmacol Exp Ther. 339(2):474-86.
2. Michalon A, et al. Chronic pharmacological mGlu5 inhibition corrects fragile X in adult mice. (2012) Neuron. 74(1):49-56.