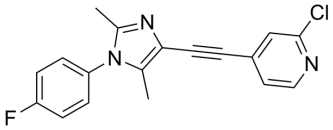
Basimglurant

Cat. No.:	HY-15446
CAS No.:	802906-73-6
Molecular Formula:	$C_{18}H_{13}ClFN_3$
Molecular Weight:	325.77
Target:	mGluR
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 33.33 mg/mL (102.31 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0697 mL	15.3483 mL	30.6965 mL
	5 mM	0.6139 mL	3.0697 mL	6.1393 mL
	10 mM	0.3070 mL	1.5348 mL	3.0697 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.67 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (7.67 mM); Suspended solution; Need ultrasonic and warming
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.67 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Basimglurant (RG7090) is a potent, selective and orally available mGlu5 negative allosteric modulator with a K_d of 1.1 nM[1]. Basimglurant is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

mGlu5 Receptor
1.1 nM (Kd)

In Vitro	[^{3}H]-basimglurant saturation analysis on recombinant human mGlu5 reveals monophasic saturation isotherms with K_d of 1.1 nM. In competition binding experiments on human recombinant mGlu5, Basimglurant (RG7090) fully displaces [^{3}H]-MPEP with a K_i of 35.6 nM and [^{3}H]-ABP688 with a K_i of 1.4 nM. In HEK293 cells stably expressing human mGlu5, Basimglurant (RG7090) inhibits quisqualate induced Ca^{2+} mobilization with an IC_{50} of 7.0 nM and [^{3}H]-inositolphosphate accumulation with an IC_{50} of 5.9 nM. Basimglurant (RG7090) shows similar potencies in radioligand binding and functional assay on human and rodent mGlu5 receptor orthologues[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Basimglurant (RG7090) is a potent, selective, and safe mGlu5 inhibitor with good oral bioavailability and long half-life supportive of once-daily administration, good brain penetration, and high in vivo potency. It has antidepressant properties which are corroborated by its functional magnetic imaging (fMRI) profile, as well as anxiolytic-like and antinociceptive features[1]. It is currently in phase II clinical studies for the treatment of depression and fragile X syndrome. In the Vogel conflict drinking test, Basimglurant dose dependently increases the drinking time. The total plasma exposure of efficacious doses of Basimglurant (RG7090) ranges from 5 ng/mL (0.03 mg/kg) to 37 ng/mL (0.3 mg/kg)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats: For intravenous PK, Basimglurant (RG7090) is formulated in N-methyl-pyrollidone (NMP)/saline (30%/70%) as vehicle and administered at a volume of 2 mL/kg. For oral gavage (p.o.) the compound is administered as suspension using gelatine/saline (7.5%/0.62% in water) at an administration volume of 4 mL/kg[1]. Monkey: For intravenous PK, Basimglurant (RG7090) is formulated in cyclodextrin solution as vehicle and administered at a volume of 2 mL/kg. For oral gavage (p.o.), the compound is administered in capsule (2 mg in size-2 capsules, i.e. ~0.3 mg/kg) to fasted or fed monkeys in a cross-over design[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- ACS Chem Neurosci. 2019 Nov 20;10(11):4558-4570.

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REFERENCES

[1]. Lindemann L, et al. Pharmacology of basimglurant (RO4917523, RG7090), a unique metabotropic glutamate receptor 5 negative allosteric modulator in clinical development for depression. J Pharmacol Exp Ther. 2015 Apr;353(1):213-33.

[2]. Jaeschke G, et al. Metabotropic glutamate receptor 5 negative allosteric modulators: discovery of 2-chloro-4-[1-(4-fluorophenyl)-2,5-dimethyl-1H-imidazol-4-ylethynyl]pyridine (basimglurant, RO4917523), a promising novel medicine for psychiatric diseases.

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