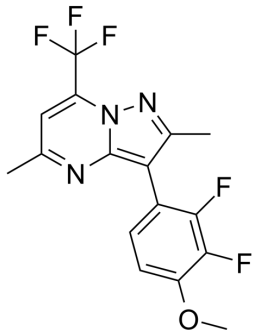
VU6005649

Cat. No.:	HY-107982
CAS No.:	2137047-43-7
Molecular Formula:	$C_{16}H_{12}F_5N_3O$
Molecular Weight:	357.28
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 : 50 mg/mL (139.95 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7989 mL	13.9946 mL	27.9893 mL
	5 mM	0.5598 mL	2.7989 mL	5.5979 mL
	10 mM	0.2799 mL	1.3995 mL	2.7989 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 (7.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

VU6005649 is a CNS penetrant $mGlu_{7/8}$ receptor agonist with EC_{50}s of 0.65 μM and 2.6 μM for $mGlu_7$ receptor and $mGlu_8$ receptor, respectively.

IC_{50} & Target

mGlu7 Receptor	mGlu8 Receptor
0.65 μM (EC50)	2.6 μM (EC50)

In Vitro

VU6005649 is a CNS penetrant $mGlu_{7/8}$ receptor agonist with EC_{50}s of 0.65 μM and 2.6 μM for $mGlu_7$ receptor and $mGlu_8$ receptor, respectively. VU6005649 displays a terminal K_p of 2.43 with total brain levels ~9× above the $mGlu_7$ positive allosteric modulator (PAM) in vitro EC_{50}[1].

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

In Vivo	When VU6005649 (compound 9f) is dosed at 30 mg/kg IP in 10% Tween 80/H_2O (0.75 mg/kg. s.c. amphetamine), no efficacy is observed in this assay. VU6005649 shows modest but significant pro-cognitive effects on associative learning in wild-type mice and the first example of efficacy of an $mGlu_{7/8}$ positive allosteric modulator (PAM) in this model[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Tissue distribution studies with VU6005649 (compound 9f) in mice are performed by formulating VU6005649 in 10% polysorbate 80 and dosing via intraperitoneal injection to 20 week old female C57/Bl6 mice (3 per time point). At 0.25, 0.5, 1, 3, and 6 hours post dose, animals are euthanized and decapitated, blood is collected via cardiac puncture and the brains are removed, thoroughly washed in cold phosphate-buffered saline, and immediately frozen on dry ice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Abe M, et al. Discovery of VU6005649, a CNS Penetrant mGlu7/8 Receptor PAM Derived from a Series of Pyrazolo[1,5-a]pyrimidines. ACS Med Chem Lett. 2017 Sep 1;8(10):1110-1115.

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