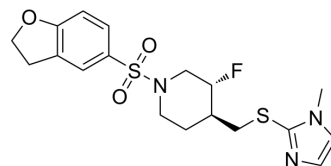


## VU6019650

Cat. No.:	HY-148502		
CAS No.:	2926782-31-0		
Molecular Formula:	C <sub>18</sub> H <sub>22</sub> FN <sub>3</sub> O <sub>3</sub> S <sub>2</sub>		
Molecular Weight:	411.51		
Target:	mAChR		
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 : 8.33 mg/mL (20.24 mM; ultrasonic and warming and heat to 60°C)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.4301 mL	12.1504 mL	24.3007 mL
	5 mM	0.4860 mL	2.4301 mL	4.8601 mL
	10 mM	0.2430 mL	1.2150 mL	2.4301 mL

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

### BIOLOGICAL ACTIVITY

#### Description

VU6019650 is a potent and selective orthosteric antagonist of M5 mAChR (IC<sub>50</sub>=36 nM), can be used for opioid use disorder (OUD) relief. VU6019650 can cross blood brain barrier, potentially modulates the mesolimbic dopaminergic reward circuitry. VU6019650 blocks Oxotremorine M iodide (HY-101372A) induced increases of neuronal firing rates of midbrain dopamine neurons in the ventral tegmental area (VTA)<sup>[1][2]</sup>.

#### IC<sub>50</sub> & Target

mAChR5  
36 nM (IC<sub>50</sub>)

#### In Vitro

VU6019650 (0-10 μM) shows high selectivity for M5 (IC<sub>50</sub>=36 nM) over other subtypes (>100-fold selectivity against human M<sub>1-4</sub>)<sup>[1]</sup>.  
VU6019650 (1 μM) blocks Oxo-M-induced activation of VTA neurons<sup>[1]</sup>.  
VU6019650 exhibits brain penetrance with rat brain and plasma K<sub>p</sub>, K<sub>p, uu</sub> values of 0.27 and 0.43, respectively<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

VU6019650 (10-56.6 mg/kg; i.p.; single dose) inhibits the rewarding effects of Oxycodone and reduces oxycodone self-

administration in rats<sup>[1]</sup>.

Pharmacokinetic Analysis in rats<sup>[1]</sup>

Route	Dose (mg/kg)	t <sub>(term)</sub> (min)	MRT (min)	Cl <sub>obs</sub> (mL/min/kg)	Vd <sub>ss</sub> (L/kg)	AUC (ng·h/mL)
i.v.	1	876	644	56.5	36.6	301

Route	Dose (mg/kg)	C <sub>max</sub> (ng/mL)	T <sub>max</sub> (h)	AUG (ng·h/mL)	F (%)
p.o.	10	433	0.25	830	27.6

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

Animal Model:	Oxycodone-induced rats <sup>[1]</sup>
Dosage:	10 mg/kg, 30 mg/kg, and 56.6 mg/kg in 10% Tween
Administration:	Intraperitoneal injection; single dose
Result:	Dose dependently reduced the number of reinforcers earned when Oxycodone is self-administered at a dose of 56.6 µg/kg/infusion.

## REFERENCES

[1]. Garrison AT, et al. Development of VU6019650: A Potent, Highly Selective, and Systemically Active Orthosteric Antagonist of the M5 Muscarinic Acetylcholine Receptor for the Treatment of Opioid Use Disorder. *J Med Chem.* 2022 Apr 28;65(8):6273-6286.

[2]. Capstick RA, et al. Discovery of a potent M5 antagonist with improved clearance profile. Part 1: Piperidine amide-based antagonists. *Bioorg Med Chem Lett.* 2022 Nov 15;76:128988.

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

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA