Product Data Sheet

Product Name: VU0364572 (trifluoroacetate salt)
Cat. No.: GC17885

Chemical Properties

Cas. No.	1240514-89-9		
Chemical Name	(3R)-3-[(2-methylbenzoyl)amino]-[1,4'-bipiperidine]-1'-carboxylic acid, ethyl ester, 2,2,2-trifluoroacetate		
SMILES	CC1=C(C(N[C@@H]2CCCN(C3CCN(C(OCC)=O)CC3)C2)=O)C=CC=C1.OC(C(F)(F)F)=O		
Formula	$C_{21}H_{31}N_3O_3 \cdot CF_3COOH$	M.Wt	487.5
Solubility	≤25mg/ml in ethanol;14mg/ml in DMSO;16mg/ml in dimethyl formamide	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			

Background

IC50: 477 ± 172 nM

VU0364572 is a M1 agonist.

Alzheimer's disease (AD) is the leading cause of dementia worldwide, and no disease-modifying therapy is availables. Selective M1 muscarinic acetylcholine receptor activation is an attractive mechanism for AD therapy since M1 mediates key effects on cognition, memory, and behavior and has potential for disease-modifying effects on Aβ formation and tau phosphorylation.

In vitro: Previous study found that VU0364572 could completely displace [(3)H]-NMS binding to the orthosteric site of M(1)-M(5) receptors at high concentrations. Moreover, consistent with previous studies suggesting actions at a site that is distinct from the

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orthosteric binding site, VU0364572 was able to slow the rate of [(3)H]-NMS dissociation from CHO-rM(1) membranes [1].

In vivo: To validate M1 as a neuroprotective treatment target for AD, VU0364572 was chronically dosed to 5XFAD mice from a young age preceding Aβ pathology to an age where these mice are known to display memory impairments. Results showed that VU0364572 could significantly decrease oligomeric (oAβ) levels in the cortex, demonstrating one mechanism whereby VU0364572 might exert its neuroprotective effects by reducing the available oAβ pool in the brain. These findings suggested that chronic M1 activation has neuroprotective potential for preventing memory impairments and reducing neuropathology in AD [2].

Clinical trial: So far, no clinical study has been conducted.

References:
[1] Digby GJ et al. Chemical modification of the M(1) agonist VU0364572 reveals molecular switches in pharmacology and a bitopic binding mode. ACS Chem Neurosci. 2012 Dec 19;3(12):1025-36.
[2] Lebois EP et al. Disease-Modifying Effects of M1 Muscarinic Acetylcholine Receptor Activation in an Alzheimer's Disease Mouse Model. ACS Chem Neurosci. 2017 Mar 7. doi: 10.1021/acschemneuro.6b00278.