Product Data Sheet

Product Name: MARK-IN-2
Cat. No.: GC31280

Chemical Properties

Cas. No.	1314893-26-9		
SMILES	O=C(C1=CC(C2=C3N=CC(Cl)=CN3N=C2)=C(C)S1)N[C@H]4C(F)(F)CCC[C@H]4N		
Formula	$C_{18}H_{18}ClF_2N_5OS$	M.Wt	425.88
Solubility	DMSO : 25 mg/mL (58.70 mM; Need ultrasonic)	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	MARK-IN-2		

Protocol

Cell experiment:

The cell biochemical potency of the below described MARK inhibitors (e.g., MARK-IN-2) is evaluated by measuring their ability to block the phosphorylation of Tau at S262 in primary cell culture of rat cortical neurons induced by the action of Okadaic acid[1].

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Animal experiment:

Rats[1]Male Sprague-Dawley Rats are via a previously implanted venous catheter at 1 mL/kg and by gastric gavage at 5 mL/kg. Male Beagle Dogs are dosed via a saphenous vein indwelling catheter at 0.5 mL/kg and by gastric gavage at 5 mL/kg. Blood samples are collected into tubes containing EDTA at pre-dose and at 5 (intravenously administered drugs only), 15, and 30 min and 1, 2, 4, 6, 8, 12, and 24 h after drug administration. After sampling, whole blood is centrifuged at 14,000 rpm for 5 min, and plasma was stored frozen at -20ºC until the day of analysis[1].

References:

[1]. Sloman DL, et al. Optimization of microtubule affinity regulating kinase (MARK) inhibitors with improved physical properties. Bioorg Med Chem Lett. 2016 Sep 1;26(17):4362-6.

Background

MARK-IN-2 is a potent microtubule affinity regulating kinase (MARK) inhibitor with an IC50 of 5 nM.

MARK-IN-2 (Compound 27) is a potent MARK inhibitor. Inhibition of MARK represents a potentially attractive means of arresting neurofibrillary tangle pathology in Alzheimer's disease. MARK-IN-2 inhibits MARK3 with an IC50 of 5 nM. MARK-IN-2 also inhibits MARK3 in primary cell culture of rat cortical neurons with an IC50 of 280 nM[1].

Characterization of the i.v. pharmacokinetic properties of MARK-IN-2 in rat and dog reveals reasonable volumes of distribution but moderate to high clearance and short

half-lives. MARK-IN-2 (Compound 27) has moderate terminal elimination half-life (t1/2=0.7 h, and 1 h for rat and dog) [1].

[1]. Sloman DL, et al. Optimization of microtubule affinity regulating kinase (MARK) inhibitors with improved physical properties. Bioorg Med Chem Lett. 2016 Sep 1;26(17):4362-6.