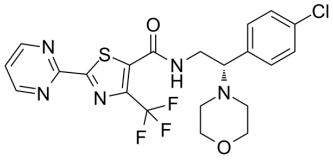
Lu AF27139

Cat. No.:	HY-132981
CAS No.:	2097117-06-9
Molecular Formula:	$C_{21}H_{19}ClF_3N_5O_2S$
Molecular Weight:	497.92
Target:	P2X Receptor
Pathway:	Membrane Transporter/Ion Channel
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 : 125 mg/mL (251.04 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0084 mL	10.0418 mL	20.0835 mL
5 mM	0.4017 mL	2.0084 mL	4.0167 mL
10 mM	0.2008 mL	1.0042 mL	2.0084 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: ≥ 2.08 mg/mL (4.18 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.18 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.18 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Lu AF27139 is a potent, selective, and orally active antagonist of P2X7 receptor (IC_{50}s of 12 and 2.4 nM for human and rat, K_is of 22, 54, and 13 nM for mouse, human, and rat, respectively). Lu AF27139 has rodent-active and CNS-penetrant character. Lu AF27139 has the potential for the research of CNS diseases[1].

IC_{50} & Target

P2X7[1]

In Vitro

Lu AF27139 (compound 1) (10-200 nM) inhibits 100 μM BzATP-induced current in HEK293 cells stably transfected with the rat

P2X7R in a dose response manner with an IC_{50} of 66 nM[1].
Lu AF27139 (compound 1) (100 nM) inhibits 300 μM BzATPinduced current in primary rat microglia with 80% inhibition occurring at a 100 nM dose[1].
Lu AF27139 (compound 1) inhibits LPS-primed and BzATP-induced IL-1β release from THP-1 cells with an IC_{50} of 38 ± 2.5 nM [1].
Lu AF27139 (compound 1) concentration-dependently blocks IL-1β release in rat and mouse primary cortical microglia primed with LPS and induces with 1 mM BzATP with IC50's of 38 ± 19 nM in rat and 26 ± 6 nM in mice[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Lu AF27139 (compound 1) (p.o.; 3, 10, and 100 mg/kg) reduces intracerebroventricular (icv) administered LPS-primed and BzATP-triggered IL-1β release in the frontal cortex of rats and mice[1].
Assessment of Pharmacokinetics (PK) profile of Lu AF27139 (compound 1) in rat[1].

dose	$C_{u, plasma}$ (nM)[a]		$C_{u, brain}$ (nM)[a]		$C_{u, spinal\ cord}$ (nM)[a]	
(mg/kg, po)	(1 h)	(2 h)	(1 h)	(2 h)	(1 h)	(2 h)
T_1	22.4 ± 4.2	22.8 ± 10	5.4 ± 2.6	6.4 ± 2.0	5.20 ± 0.80	10.0 ± 2.0

a: Free plasma, brain, and spinal cord concentrations of Lu AF27139 in rat were determined by the formula ($Ct*f_u$), where Ct is the total tissue (plasma, brain, or spinal cord) drug concentration and f_u is the fraction unbound in these tissues as determined by ex vivo equilibrium dialysis. Values are expressed as mean ± SEM for n = 3 animals. f_u, plasma = 0.02 ± 0.00, f_u, spinal cord = 0.07 ± 0.03, and f_u, brain = 0.09 ± 0.03. Values are expressed as mean ± SEM for n ≥ 3 experiments.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague–Dawley rats (280–350 g); Male C57BL mice (18–25g)[1]
Dosage:	3, 10, and 100 mg/kg
Administration:	p.o.
Result:	Reduced intracerebroventricular (icv) administered LPS-primed and BzATP-triggered IL-1β release in the frontal cortex of rats and mice.

REFERENCES

[1]. Hopper AT, et al. Synthesis and Characterization of the Novel Rodent-Active and CNS-Penetrant P2X7 Receptor Antagonist Lu AF27139. J Med Chem. 2021;64(8):4891-4902.

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

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