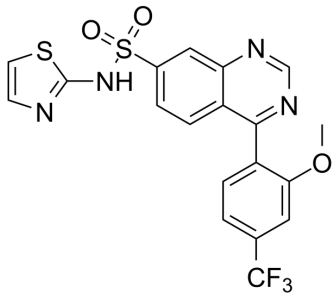
AM-2099

Cat. No.:	HY-100727
CAS No.:	1443373-17-8
Molecular Formula:	$C_{19}H_{13}F_3N_4O_3S_2$
Molecular Weight:	466.46
Target:	Sodium Channel
Pathway:	Membrane Transporter/Ion Channel
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 : ≥ 150 mg/mL (321.57 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1438 mL	10.7190 mL	21.4381 mL
	5 mM	0.4288 mL	2.1438 mL	4.2876 mL
	10 mM	0.2144 mL	1.0719 mL	2.1438 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 (5.36 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AM-2099 is a potent and selective inhibitor of voltage-gated sodium channel Nav1.7 with an IC_{50} of 0.16 μM for human Nav1.7.

IC_{50} & Target

IC50: 0.16 μM (human Nav1.7), 0.18 μM (mouse Nav1.7), 3.5 μM (rat Nav1.7) [1]

In Vitro

In heterologous cells, comparable inhibition is observed across human, mouse, dog, and cynomolgus monkey NaV1.7 with reduced activity against rat NaV1.7. AM-2099 is more than 100-fold selective over Nav1.3, Nav1.4, Nav1.5, and Nav1.8, while lower levels of selectivity are observed against Nav1.1, Nav1.2, and Nav1.6. AM-2099 demonstrates low affinity for hERG (>30 μM) and does not show greater than 50% inhibition against a panel of 100 kinases (1 μM) and a broad CEREP panel (10 μM).

	[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AM-2099 demonstrates a favorable pharmacokinetic profile in rat and dog. In rats AM-2099 shows low total clearance and moderate Vdss and half-life. In contrast, when dosed in dogs AM-2099 shows very low clearance, a low Vdss and long halflife (18 h). AM-2099 demonstrates a dose-dependent increase in plasma exposure with a concomitant dose-dependent reduction in scratching bouts compared to vehicle-treated animals, with a statistically significant reduction observed at the 60 mg/kg dose[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: AM-2099 (5, 20, 60 mg/kg) is dosed orally to C57BL/6 male mice 120 minutes prior to intradermal administration of histamine. Instances of scratching behavior are then measured over a 30-minute time period[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Marx IE, et al. Sulfonamides as Selective NaV1.7 Inhibitors: Optimizing Potency and Pharmacokinetics to Enable in Vivo Target Engagement. ACS Med Chem Lett. 2016 Sep 21;7(12):1062-1067.

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