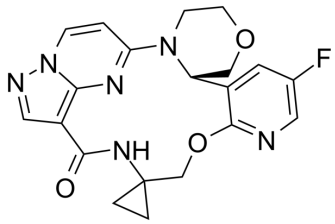
LPM4870108

Cat. No.:	HY-132229
CAS No.:	2803679-07-2
Molecular Formula:	$C_{20}H_{19}FN_6O_3$
Molecular Weight:	410.4
Target:	Trk Receptor
Pathway:	Neuronal Signaling; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

LPM4870108 is a potent and orally active pan-Trk (WT and MT) inhibitor, with IC_{50}s of 0.2 nM, 2.4 nM, 3.5 nM and 2.3 nM for TrkC, TrkA, $TrkA^{G595R}$ and $TrkA^{G667C}$, respectively. LPM4870108 shows selectivity for Trk over ALK (IC_{50}=182 nM). LPM4870108 exhibits anti-tumor activity[1][2].

IC_{50} & Target

TrkC	TrkA
0.2 nM (IC_{50})	2.4 nM (IC_{50})

In Vitro

LPM4870108 (compound 10) inhibits the activities of TrkA, TrkB, and TRC with high selectivity at 0.5 μM (kinase activity remaining, <10%) and slightly inhibit the activities of ALK and ROS1 (kinase activity remaining, 10-30%)[1].

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

In Vivo

LPM4870108 (compound 10) (5-20 mg/kg; p.o. once daily for 21 days) inhibits tumor growth in BaF3-NTRK xenograft tumor models[1].

LPM4870108 (2 mg/kg; a single i.v.) exhibits terminal half-life ($t_{1/2}$) (male 0.87 h, 2.21 h), the Cl (male 19.3 mL/kg/min, female 8.19 mL/kg/min), and the AUC_{0-t} (male 4191 nM•h, female 10282 nM•h) in rats[1].

LPM4870108 (10 mg/kg; a single p.o.) exhibits oral bioavailability (male 56.0%, female 61.9%), C_{max} (male 6384 nM, female 6628 nM) and T_{max} (male 0.667 h, female 0.667 h) in rats[1].

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

Animal Model:	Mice bearing 100-200 mm^3 BaF3-NTRK tumors[1]
Dosage:	5, 10, 20 mg/kg
Administration:	P.o. once daily for 21 days
Result:	Showed slight weight loss and all animals survived at the highest dose.

Animal Model:	Sprague-Dawley rats (six males and six females)[1]
Dosage:	2 mg/kg for i.v.; 10 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous administration and oral administration

Result:	I.v.: $t_{1/2}$ (male 0.87 h, 2.21 h), Cl (male 19.3 mL/kg/min, female 8.19 mL/kg/min), AUC_{0-t} (male 4191 nM•h, female 10282 nM•h). P.o.: F (male 56.0%, female 61.9%), C_{max} (male 6384 nM, female 6628 nM), T_{max} (male 0.667 h, female 0.667 h).

REFERENCES

[1]. Liu Z, et, al. Discovery of the Next-Generation Pan-TRK Kinase Inhibitors for the Treatment of Cancer. J Med Chem. 2021 Jul 22;64(14):10286-10296.

[2]. Duan S, et, al. Assessment of the toxicity and toxicokinetics of the novel potent tropomyosin receptor kinase (Trk) inhibitor LPM4870108 in rhesus monkeys. Regul Toxicol Pharmacol. 2021 Jun;122:104886.

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