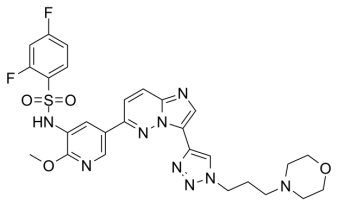
PI3K/mTOR Inhibitor-12

Cat. No.:	HY-152238
CAS No.:	2891692-83-2
Molecular Formula:	$C_{27}H_{27}F_2N_9O_4S$
Molecular Weight:	611.62
Target:	PI3K; mTOR
Pathway:	PI3K/Akt/mTOR
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PI3K/mTOR Inhibitor-12 is a potent, orally active and selective PI3K/mTOR inhibitor with IC_{50} values of 0.06 nM and 3.12 nM for PI3Kα and mTOR, respectively. PI3K/mTOR Inhibitor-12 has antitumor activity. PI3K/mTOR Inhibitor-12 has lower liver toxicity[1].

IC_{50} & Target

PI3Kα	mTOR
0.06 nM (IC_{50})	3.12 nM (IC_{50})

In Vitro

PI3K/mTOR Inhibitor-12 (compound 48; 72 h) inhibits cancer cells growth with IC_{50} values of 0.07, 0.09, 0.54, 0.54, and 0.68 μM for PC-3, HT-29,HCT116, LOVO, and HUVEC cells, respectively[1].

PI3K/mTOR Inhibitor-12 (0.25-1 μM; 12-48 h; HCT116 and HT-29 cells) inhibits the activation of PI3K and mTOR in the cellular context[1].

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

Western Blot Analysis[1]

Cell Line:	HCT116 and HT-29 cells
Concentration:	0.25, 0.5, and 1 μM
Incubation Time:	12, 24, and 48 hours
Result:	Inhibited the expression levels of AKT, p70S6K and their phosphorylated forms in a dose- and time-dependent manner.

In Vivo

PI3K/mTOR Inhibitor-12 (compound 48; 20 mg/kg; p.o.; daily, for 14 d) inhibits tumor growth of HCT116 xenografts in female BALB/c nude mice[1].

PI3K/mTOR Inhibitor-12 (1 and 5 mg/kg; i.v. and p.o.; male SD rats) has fast plasma clearance (1428 mL/h/kg) and short $T_{1/2}$ (2.33 h) and the $AUC_{0-\infty}$ is 1356 h*ng/mL[1].

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

Animal Model:	HCT116 xenografts in female BALB/c nude mice[1]
Dosage:	20 mg/kg

Administration:	Oral administration, daily, for 14 days
Result:	Reduced the growth of HCT116 tumors, and the tumor growth inhibition (TGI) was 73.33%. Had lower liver toxicity of HCT116 xenografts in female BALB/c nude mice.

Animal Model:	Male SD rats[1]
Dosage:	1 and 5 mg/kg
Administration:	Intravenous injection (1 mg/kg) and oral administration (5 mg/kg)

Result:

Parameter	I.V. (1 mg/kg)	Parameter	P.O. (5 mg/kg)
$T_{1/2}$ (h)	0.6	$T_{1/2}$ (h)	2.33
CL (mL/h/kg)	1428	C_{max} (ng/mL)	1218
Vdss (mL/Kg)	528	$AUC_{0-\infty}$ (h*ng/mL)	1356
$AUC_{0-\infty}$ (h*ng/mL)	760	F%	33.1

REFERENCES

[1]. Li C, et, al. Function-oriented synthesis of Imidazo[1,2-a]pyrazine and Imidazo[1,2-b]pyridazine derivatives as potent PI3K/mTOR dual inhibitors. Eur J Med Chem. 2022 Dec 20;247:115030.

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