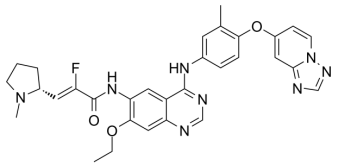
SPH5030

Cat. No.:	HY-143319
CAS No.:	2364326-23-6
Molecular Formula:	$C_{31}H_{31}FN_8O_3$
Molecular Weight:	582.63
Target:	Others
Pathway:	Others
Storage:	4°C, protect from light, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (171.64 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7164 mL	8.5818 mL	17.1636 mL
	5 mM	0.3433 mL	1.7164 mL	3.4327 mL
	10 mM	0.1716 mL	0.8582 mL	1.7164 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

SPH5030 is a selective and irreversible HER2 inhibitor. SPH5030 inhibits $HER2^{WT}$ and $EGFR^{WT}$ with IC_{50}s of 3.51 and 8.13 nM, respectively. SPH5030 shows excellent activities against HER2 mutants. SPH5030 can be used for the research of cancer[1].

IC_{50} & Target

IC50: 3.51 nM ($HER2^{WT}$), 0.42 nM ($HER2^{D769H}$), 0.43 nM ($HER2^{D769Y}$), 0.16 nM ($HER2^{V777L}$), 0.56 nM ($HER2^{R896C}$), 8.13 nM ($EGFR^{WT}$)[1]

In Vitro

SPH5030 (0-10 μM; 72 h) shows anti-proliferation activities against tumor cell lines[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	NCI-N87, BT-474, SK-BR-3 with HER2 overexpression, MDA-MB-468 with EGFR overexpression, NCI-H441, Es-2, MFE-280, NUGC-4, COLO678, KM12-luc and BaF3 cell lines
Concentration:	0-10 μM

Incubation Time:	72 hours
Result:	Effectively inhibited NCI-N87, BT-474, SK-BR-3 with HER2 overexpression and BaF3 cells with IC_{50}s of 1.09, 2.01, 20.09 and 6.3 nM, respectively. Poorly inhibited MDA-MB-468 with EGFR overexpression, NCI-H441, Es-2, MFE-280, NUGC-4, COLO678 and KM12-luc cells with IC_{50}s of 2980, 4257, 2716, 3967, 1218, 6065 and 3597 nM, respectively.

In Vivo

SPH5030 (5-40 mg/kg; p.o. once per day for 13 or 21 days) shows in vivo antitumor efficacy in mice with xenograft tumor models[1].

Pharmacokinetic Properties of SPH5030 in Mice and Rats[1].

	Mice IV 3 mg/kg	Mice PO 10 mg/kg	Rats IV 3 mg/kg	Rats PO 6 mg/kg
CL (L/kg·h)	0.70±0.20		0.78±0.13	
$t_{1/2}$ (h)	3.76±0.15	3.60±0.59	4.56±0.20	4.38±0.35
V_{ss} (L/kg)	2.96±0.96		3.55±0.64	
C_{max} (μg/mL)		1.90±0.14		0.76±0.33
t_{max} (h)		2.67±1.15		3.33±1.15
AUC_{0-t} (h·μg/mL)		13.07±0.48		5.47±2.82
F (%)		87.66		71.35

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Animal Model:	BALB/c nude mouse with NCI-N87 and BT474 xenografts, and NPSG mouse with BAF3 HER2 A775_G776insYVMA xenografts[1]
Dosage:	5, 10, 20 and 40 mg/kg
Administration:	Oral gavage; 5-40 mg/kg once per day; for 13 or 21 days
Result:	Dose-dependently inhibited tumor growth in NCI-N87, BT474 and BAF3 HER2 A775_G776insYVMA xenograft mouse models, and showed an equivalent or better activity of tumor inhibition compared with neratinib and pyrotinib at a dose of 20 mg/kg. Showed no mortality or significant loss of body weight in xenograft mouse models.

REFERENCES

[1]. Li D,et al. Discovery of SPH5030, a Selective, Potent, and Irreversible Tyrosine Kinase Inhibitor for HER2-Amplified and HER2-Mutant Cancer Treatment. J Med Chem. 2022 Apr 14;65(7):5334-5354.

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

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