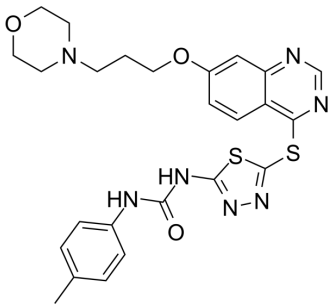
SKLB4771

Cat. No.:	HY-12960
CAS No.:	1370256-78-2
Molecular Formula:	$C_{25}H_{27}N_7O_3S_2$
Molecular Weight:	537.66
Target:	FLT3
Pathway:	Protein Tyrosine Kinase/RTK
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 : 33.33 mg/mL (61.99 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8599 mL	9.2996 mL	18.5991 mL
	5 mM	0.3720 mL	1.8599 mL	3.7198 mL
	10 mM	0.1860 mL	0.9300 mL	1.8599 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 (4.65 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.65 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.65 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SKLB4771 is a novel potent and selective Flt3 inhibitor with IC50 of 10 nM; against FLT3-ITD-expressing MV4-11 cells with IC50 of 6 nM.IC50 value: 10 nM (in vitro) [1]Target: in vitro: SKLB4771 inhibited FLT3 phosphorylation in a dose-dependent manner. Consistent with the downregulation of the phosphorylation of FLT3, the phosphorylation of the downstream signaling proteins STAT5 and ERK1/2 was also significantly inhibited at concentrations >0.1 μM. SKLB4771 potently inhibited the growth of MV4-11 cells that express FLT3-ITD, with an IC50 value of 0.006 μM. It just exhibited very weak inhibitory activity against human T lymphoma Jurkat cells, human Burkitt's lymphoma Ramos cells, human lung cancer PC-9 and H292 cells, and human epithelial carcinoma A431 cells (IC50: 3.05 μM, 6.25 μM, 3.72 μM, 6.94 μM, and 8.91 μM, respectively).

For other leukemia and solid tumor cell lines, including K562, U937, Karpas299, HCC827, A549, H2228, H820, MDA-MB-231, BT474, MCF-7, HCT116, SW480, LoVo, HeLa, SKOV-3, SK, DU145, PC-3, A431, and SH-SY5Y [1].in vivo: Treatment with SKLB4771 at 100 mg/kg/d resulted in rapid and complete tumor regression in all mice of this group. SKLB4771 treatment at 20 mg/kg/d and 40 mg/kg/d significantly slowed down the tumor growth; the tumor inhibition rates are 66% and 84%, respectively. Moreover, during the whole experiment, no significant weight loss or any other obvious signs of toxicity were observed for all of the SKLB4771 treated mice.

REFERENCES

[1]. Li WW, et al. Discovery of the novel potent and selective FLT3 inhibitor 1-{5-[7-(3- morpholinopropoxy)quinazolin-4-ylthio]-[1,3,4]thiadiazol-2-yl}-3-p-tolylurea and its anti-acute myeloid leukemia (AML) activities in vitro and in vivo. J Med Chem. 2012 Apr 26;55(8):3852-66.

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