产品名称：**S49076**
产品别名：**S49076**

生物活性：

Description	S49076 is a novel, potent inhibitor of **MET**, **AXL/MER**, and **FGFR1/2/3** with **IC_{50}** values below 20 nM.					
IC_{50} & Target	MET^{D1246N}	MET^{Y1248C}	MET^{D1246H}	MET^{Y1248D}	MET^{Y1248H}	MET^{M1268T}
	8 nM (IC_{50})	16 nM (IC_{50})	11 nM (IC_{50})	17 nM (IC_{50})	1 nM (IC_{50})	1 nM (IC_{50})
	MET	FGFR1	$FGFR1^{V561M}$	FGFR2	$FGFR2^{N549H}$	FGFR3
	1 nM (IC_{50})	18 nM (IC_{50})	23 nM (IC_{50})	17 nM (IC_{50})	19 nM (IC_{50})	15 nM (IC_{50})
	AXL	MER				
	7 nM (IC_{50})	2 nM (IC_{50})				
In Vitro	S49076 potently blocks cellular phosphorylation of MET, AXL, and FGFRs and inhibits downstream signaling. S49076 inhibits the proliferation of MET- and FGFR2-dependent gastric cancer cells, blocks MET-driven migration of lung carcinoma cells, and inhibits colony formation of hepatocarcinoma cells expressing FGFR1/2 and AXL. Total inhibition of MET phosphorylation is seen after 2 hours of incubation with 10 nM S49076 and an with an IC50 of 2 nM. S49076 inhibits MET phosphorylation on this site in GTL-16 gastric carcinoma cells with an IC50 value of 3 nM. The IC50 for AXL inhibition by S49076 is 56 nM. S49076 inhibits AXL signaling via AKT with an IC50 of 33 nM[1].					
In Vivo	In tumor xenograft models, a good pharmacokinetic/pharmacodynamic relationship for MET and FGFR2 inhibition following oral administration of S49076 is established and correlated well with impact on tumor growth. MET, AXL, and the FGFRs have all been implicated in resistance to VEGF/VEGFR inhibitors such as bevacizumab. Combination of S49076 with bevacizumab in colon carcinoma xenograft models leads to near total inhibition of tumor growth. S49076 alone caused tumor growth arrest in bevacizumab-resistant tumors[1].					
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 31 mg/mL (70.70 mM)** * "≥" means soluble, but saturation unknown.					
	Preparing Stock Solutions	**Solvent / Mass / Concentration**	**1 mg**	**5 mg**	**10 mg**	
		1 mM	2.2805 mL	11.4025 mL	22.8050 mL	
		5 mM	0.4561 mL	2.2805 mL	4.5610 mL	
		10 mM	0.2281 mL	1.1403 mL	2.2805 mL	
	*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。 储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。					
References	[1]. Burbridge MF, et al. S49076 is a novel kinase inhibitor of MET, AXL, and FGFR with strong preclinical activity alone and in association with bevacizumab. Mol Cancer Ther. 2013 Sep;12(9):1749-62.					

实验参考：

	For GTL-16 and SNU-16 viability assays, cells are seeded in 96-well microplates at the appropriate density in media containing 10% FCS and supplemented 48 hours later with serial dilutions of

Cell Assay	S49076 in a final volume of 150 µL per well. After 96 hours (GTL-16) or 120 hours (SNU-16) incubation (corresponding to 4 doubling times), 15 µL of a solution of 5 mg/mL MTT is added to each well and the plates are incubated for 4 hours at 37°C. The formazan metabolite is solubilized in SDS for SNU-16 and, following removal of the MTT solution, in DMSO for GTL-16. Global cell viability is estimated by measurement of optical density at 540 nm[1].
Animal Administration	Mice: Female balb/c and swiss nu/nu mice are used in the study. The hydrochloride salt of S49076 is administered orally to mice in 1% (w/v) hydroxyethylcellulose in ammonium acetate buffer pH 4.5 in a volume of 200 µL per 20 g body weight. The maximal tolerated dose of S49076 in these mice is determined to be 100 mg/kg/d (5 days a week for at least 3 weeks). Bevacizumab is dissolved in PBS and administered intraperitoneally in a volume of 200 µL per 20 g body weight[1].
References	[1]. Burbridge MF, et al. S49076 is a novel kinase inhibitor of MET, AXL, and FGFR with strong preclinical activity alone and in association with bevacizumab. Mol Cancer Ther. 2013 Sep;12(9):1749-62.