产品名称：Golvatinib(E7050)
产品别名：Golvatinib；E-7050

生物活性：

Description	Golvatinib (E-7050) is a potent dual inhibitor of both c-Met and VEGFR2 kinases with IC_{50}s of 14 and 16 nM, respectively.	
IC_{50} & Target	VEGFR2	c-Met
	16 nM (IC_{50})	14 nM (IC_{50})
In Vitro	Golvatinib (E-7050) potently inhibits phosphorylation of both c-Met and VEGFR-2. Golvatinib also potently represses the growth of both c-met amplified tumor cells and endothelial cells stimulated with either HGF or VEGF. Golvatinib strongly inhibits the growth of MKN45, EBC-1, Hs746T, and SNU-5 tumor cells with IC50 values of 37, 6.2, 23, and 24 nM, respectively. The growth of A549, SNU-1 and 0MKN74 tumor cells is inhibited by Golvatinib with much higher IC50 values[1]. Golvatinib circumvents resistance to all of the reversible, irreversible, and mutant-selective EGFR-TKIs induced by exogenous and/or endogenous HGF in EGFR mutant lung cancer cell lines, by blocking the Met/Gab1/PI3K/Akt pathway in vitro. Golvatinib also prevents the emergence of gefitinib-resistant HCC827 cells induced by continuous exposure to HGF[2].	
In Vivo	Golvatinib (E-7050) shows inhibition of the phosphorylation of c-Met and VEGFR-2 in tumors, and strong inhibition of tumor growth and tumor angiogenesis in xenograft models. Treatment of some tumor lines containing c-met amplifications with high doses of Golvatinib (50-200 mg/kg) induced tumor regression and disappearance. In a peritoneal dissemination model, Golvatinib shows an antitumor effect against peritoneal tumors as well as a significant prolongation of lifespan in treated mice[1]. Golvatinib (E7050) plus Gefitinib results in marked regression of tumor growth associated with inhibition of Akt phosphorylation in cancer cells[2].	
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL (78.90 mM;** Need ultrasonic)	

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5781 mL	7.8903 mL	15.7806 mL
	5 mM	0.3156 mL	1.5781 mL	3.1561 mL
	10 mM	0.1578 mL	0.7890 mL	1.5781 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。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出

	现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 3 mg/mL (4.73 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (4.73 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 30.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 3 mg/mL (4.73 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (4.73 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: 3 mg/mL (4.73 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (4.73 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Nakagawa T et al. E7050: a dual c-Met and VEGFR-2 tyrosine kinase inhibitor promotes tumor regression and prolongs survival in mouse xenograft models. Cancer Sci, 2010, 101(1), 210-215. [2]. Wang W et al. Met kinase inhibitor E7050 reverses three different mechanisms of hepatocyte growth factor-induced tyrosine kinase inhibitor resistance in EGFR mutant lung cancer. Clin Cancer Res, 2012, 18(6), 1663-1671.

实验参考：

Cell Assay	Cells (1000-3000 cells/100 μL/well) are seeded on 96-well culture plates with various concentrations of Golvatinib and cultured for 3 days. Then, 10 μL of WST-8 reagent is added to each well, and absorbance is measured at 450 nm compared with a reference measurement at 660 nm using a MTP-500 microplate reader[1]
Animal Administration	Mice: Nude mice bearing MKN45, Hs746T, SNU-5, or EBC-1 tumors are administered Golvatinib (25, 50, 100, 200 mg/kg) or vehicle only as a control, once a day. Tumor volume is measured using calipers on the indicated days (0-15 days) [1]
References	[1]. Nakagawa T et al. E7050: a dual c-Met and VEGFR-2 tyrosine kinase inhibitor promotes tumor regression and prolongs survival in mouse xenograft models. Cancer Sci, 2010, 101(1), 210-215. [2]. Wang W et al. Met kinase inhibitor E7050 reverses three different mechanisms of hepatocyte growth factor-induced tyrosine kinase inhibitor resistance in EGFR mutant lung cancer. Clin Cancer Res, 2012, 18(6), 1663-1671.