产品名称：**G007-LK**
产品别名：**G007-LK**

生物活性：

Description	G007-LK is a potent and selective inhibitor of **TNKS1** and **TNKS2**, with **IC_{50}**s of 46 nM and 25 nM, respectively.	
IC_{50} & Target	TNKS2	TNKS1
	25 nM (IC_{50})	46 nM (IC_{50})
In Vitro	G007-LK is a potent inhibitor of TNKS1 and TNKS2, with IC50s of 46 nM and 25 nM, respectively, and a cellular IC50 of 50 nM. G007-LK shows no inhibition of PARP1 at doses up to 20 μM, and has a high CYP3A4 inhibition IC50 value (>25 μM)[1]. G007-LK (0-20 μM) dose-dependently inhibits hepatocellular carcinoma (HCC) cell growth. G007-LK also downregulates the levels of YAP by upregulating AMOTL1 and AMOTL2 in HCC cell lines. In addition, G007-LK (0-20 μM) synergizes with MEK and AKT inhibitors to suppress HCC cell proliferation[3].	
In Vivo	G007-LK displays great pharmacokinetic profile in ICR mice[1]. G007-LK (100 mg/kg chow, p.o.) significantly reduces lineage tracing from LGR5+ intestinal stem cells in mice. G007-LK (100 mg/kg chow, p.o.) specifically targets LGR5+ WNT-dependent intestinal stem cells in Lgr5-EGFP-CreERT2;R26R-tdTomato mice. G007-LK (10, 50 mg/kg, p.o.) also suppressses canonical WNT signalling. Furthermore, G007-LK (100, 1000 mg/kg chow, p.o) shows no effect on the alteration of duodenal morphology[2].	
Solvent&Solubility	***In Vitro:*** **DMSO： ≥ 30 mg/mL (56.61 mM)** * "≥" means soluble, but saturation unknown.	

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8869 mL	9.4347 mL	18.8693 mL
	5 mM	0.3774 mL	1.8869 mL	3.7739 mL
	10 mM	0.1887 mL	0.9435 mL	1.8869 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]. Voronkov A, et al. Structural basis and SAR for G007-LK, a lead stage 1,2,4-triazole based specific tankyrase 1/2 inhibitor. J Med Chem. 2013 Apr 11;56(7):3012-23.

[2]. Norum JH, et al. The tankyrase inhibitor G007-LK inhibits small intestine LGR5+ stem cell proliferation without altering tissue morphology. Biol Res. 2018 Jan 9;51(1):3.

[3]. Xin Chen, et al. Tankyrase inhibitors suppress hepatocellular carcinoma cell growth via modulating the Hippo cascade. PLoS One. 2017 Sep 6;12(9):e0184068.

实验参考：

Cell Assay	For cell proliferation or apoptosis assays, SNU-449 and HLE cells are grown in a 5% CO2 atmosphere, at 37°C, in RPMI Medium supplemented with 10% fetal bovine serum (FBS) and penicillin/streptomycin. HCC cells are treated with 0.1% DMSO, or 2.5 μM, 5 μM, 10 μM, 20μM

	XAV-939 or G007-LK, either alone or in combination with the MEK inhibitor U0126 (25 μM) or the AKT inhibitor MK-2206 (5 μM). Cell proliferation is analyzed using the BrdU Cell Proliferation Assay Kit, while apoptosis is assessed with the Cell Death Detection Elisa Plus Kit[3].
Animal Administration	Drug treatment experiments are performed with wild type (wt), single or double transgenic Lgr5-EGFP-Ires-CreERT2;R26R-Confetti mice, unless indicated otherwise. G007-LK is administered orally either by gavage (10 or 50 mg/kg body mass once daily, vehicle: 15% dimethylsulfoxide [DMSO], 17.5% Cremophor EL, 8.75% Miglyol 810 N, 8.75% ethanol in phosphate buffered saline [PBS]) or in G007-LK enriched chow (100 or 1000 mg G007-LK/kg chow ad libitum, corresponding to a daily G007-LK dose of approximately 20 or 200 mg/kg body mass, respectively, for a mouse with a body mass of 25 g and consumption of approximately 5 g enriched diet/day). G007-LK treatments are initiated at the age of 5 weeks and 5 days for oral gavage treatment or 6 weeks for enriched chow administration and continued for 9 or 21 days, respectively[2].
References	[1]. Voronkov A, et al. Structural basis and SAR for G007-LK, a lead stage 1,2,4-triazole based specific tankyrase 1/2 inhibitor. J Med Chem. 2013 Apr 11;56(7):3012-23. [2]. Norum JH, et al. The tankyrase inhibitor G007-LK inhibits small intestine LGR5+ stem cell proliferation without altering tissue morphology. Biol Res. 2018 Jan 9;51(1):3. [3]. Xin Chen, et al. Tankyrase inhibitors suppress hepatocellular carcinoma cell growth via modulating the Hippo cascade. PLoS One. 2017 Sep 6;12(9):e0184068.