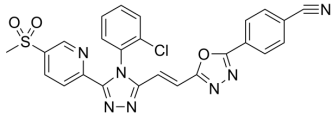
G007-LK

Cat. No.:	HY-12438
CAS No.:	1380672-07-0
Molecular Formula:	$C_{25}H_{16}ClN_7O_3S$
Molecular Weight:	529.96
Target:	PARP
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (3.92 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.92 mM); Clear solution

BIOLOGICAL ACTIVITY

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 IC_{50}s of 46 nM and 25 nM, respectively, and a cellular IC_{50} of 50 nM. G007-LK shows no inhibition of PARP1 at doses up to 20 μM, and has a high CYP3A4 inhibition IC_{50} 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	For cell proliferation or apoptosis assays, SNU-449 and HLE cells are grown in a 5% CO_2 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Discov. 2019 Oct;9(10):1358-1371.
- EMBO Mol Med. 2023 Jan 18;e16235.
- Int J Mol Sci. 2023 Apr 4, 24(7), 6733.
- Am J Cancer Res. 2022 Mar 15;12(3):1069-1087.
- Lab Invest. 2020 Jul;100(7):1003-1013.

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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.

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

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