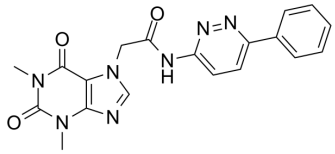
ETC-159

Cat. No.:	HY-18988
CAS No.:	1638250-96-0
Molecular Formula:	$C_{19}H_{17}N_7O_3$
Molecular Weight:	391.38
Target:	Porcupine; Wnt
Pathway:	Stem Cell/Wnt
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 : 50 mg/mL (127.75 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5551 mL	12.7753 mL	25.5506 mL
	5 mM	0.5110 mL	2.5551 mL	5.1101 mL
	10 mM	0.2555 mL	1.2775 mL	2.5551 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 (6.39 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ETC-159 (ETC-1922159) is a potent, orally available PORCN inhibitor. ETC-159 inhibits β-catenin reporter activity with an IC_{50} of 2.9 nM.

IC_{50} & Target

IC50: 2.9 nM (β-catenin)[1]

In Vitro

ETC-159 blocks the secretion and activity of all Wnts. ETC-159 has robust activity in multiple cancer models driven by high Wnt signaling. ETC-159 is highly efficacious in molecularly defined colorectal cancers (CRCs) with R-spondin translocations [1]

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	ETC-159 inhibits mouse PORCN with an IC_{50} of 18.1 nM, whereas the IC50 for Xenopus Porcn is approximately four fold higher (70 nM). ETC-159 is remarkably effective in treating RSPO-translocation bearing colorectal cancer (CRC) patient-derived xenografts. ETC-159 exhibits good oral pharmacokinetics in mice allowing preclinical evaluation via oral administration. After a single oral dose of 5 mg/kg, ETC-159 is rapidly absorbed into the blood with a T_{max} of ~0.5 h and oral bioavailability of 100%[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	HEK293 cells stably transfected with STF reporter and pPGK-WNT3A plasmid (STF3A cells) are treated with varying concentrations of compounds. For Wnt secretion, STF3A cells are treated with ETC-159 diluted in 1% fetal bovine serum-containing media[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: For human xenograft models, patient-derived solid tissue fragments are subcutaneously implanted in BALB/c nude mice. All groups are matched for tumor size with equal variance before treatment. ETC-159 formulated in 50% PEG400 (vol/vol) in water is administered by oral gavage at a dosing volume of 10 μL/g body weight[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Adv. 2020 May 22;6(21):eaaz5913.
- Am J Physiol Endocrinol Metab. 2021 Mar 15.
- PRACTICAL ONCOLOGY JOURNAL. 2018,32(02):103-106.

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REFERENCES

[1]. Madan B, et al. Wnt addiction of genetically defined cancers reversed by PORCN inhibition. Oncogene. 2015 Aug 10. doi: 10.1038/onc.2015.280.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA