ETC-159

Cat. No.: HY-18988
CAS No.: 1638250-96-0
Molecular Formula: C₁₉H₁₇N₇O₃
Molecular Weight: 391.38
Target: Wnt; Porcupine
Pathway: Stem Cell/Wnt
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 : 50 mg/mL (127.75 mM; Need ultrasonic)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.5551 mL</td>
<td>12.7753 mL</td>
<td>25.5506 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5110 mL</td>
<td>2.5551 mL</td>
<td>5.1101 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2555 mL</td>
<td>1.2775 mL</td>
<td>2.5551 mL</td>
</tr>
</tbody>
</table>

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 IC₅₀ of 2.9 nM.

IC₅₀ & 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

- Eur J Pharmacol. 2023 Feb 27;175628.
- PRACTICAL ONCOLOGY JOURNAL. 2018,32(02):103-106.

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REFERENCES