Ravoxertinib

Cat. No.: HY-15947
CAS No.: 1453848-26-4
Molecular Formula: C₂₁H₁₈ClFN₆O₂
Molecular Weight: 440.86
Target: ERK
Pathway: MAPK/ERK Pathway; Stem Cell/Wnt
Storage:
- Powder: -20°C for 3 years, 4°C for 2 years
- In solvent: -80°C for 6 months, -20°C for 1 month

SOLVENT & SOLUBILITY

In Vitro

DMSO: ≥ 35 mg/mL (79.39 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.2683 mL</td>
<td>11.3415 mL</td>
<td>22.6829 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4537 mL</td>
<td>2.2683 mL</td>
<td>4.5366 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2268 mL</td>
<td>1.1341 mL</td>
<td>2.2683 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: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.67 mg/mL (3.79 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (3.79 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Ravoxertinib (GDC-0994) is an orally active ERK kinase inhibitor with an IC₅₀ of 6.1 nM and 3.1 nM for ERK1 and ERK2, respectively.

IC₅₀ & Target
<table>
<thead>
<tr>
<th>ERK2</th>
<th>ERK1</th>
<th>p-RSK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In Vitro</td>
<td>Ravoxertinib (GDC-0994) also inhibits p90RSK with an IC\textsubscript{50} of 12 nM\textsuperscript{[1]}. Ravoxertinib (GDC-0994) is highly selective for ERK1 and ERK2, with biochemical potency of 1.1 nM and 0.3 nM, respectively \textsuperscript{[2]}, Ravoxertinib (GDC0994; 50 nM, 0.5 \mu M, and 5 \mu M; 48 hours) decreases the viability of lung adenocarcinoma cell lines (A549, HCC827, HCC4006)\textsuperscript{[3]}. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</td>
<td></td>
</tr>
<tr>
<td>In Vivo</td>
<td>In CD-1 mice, a 10 mg/kg oral dose of Ravoxertinib (GDC-0994) is sufficient to achieve the desired target coverage for at least 8 h\textsuperscript{[1]}. Daily, oral dosing of Ravoxertinib results in significant single-agent activity in multiple in vivo cancer models, including KRAS-mutant and BRAF-mutant human xenograft tumors in mice\textsuperscript{[2]}. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</td>
<td></td>
</tr>
</tbody>
</table>

**PROTOCOL**

**Animal Administration\textsuperscript{[1]}**

- **PK/PD data for Ravoxertinib (GDC-0994) in the HCT116 mouse xenograft model. HCT116 tumors are established in nude mice to a tumor volume of 400-600 mm\textsuperscript{3}. Mice are treated with a single oral dose of 22 at 15, 30, or 100 mg/kg versus vehicle control alone (40\% PEG400/60\% (10\% HP\textbeta CD)) follow by tumor and plasma collection at 2, 8, 16, and 24 h postdose. Tumor levels of phosphorylated p90RSK (pRSK) relative total p90RSK (tRSK) are measured by quantitative Western blot and are normalized to vehicle control at 2 h postdose (set to 100\%). Plasma and tumor concentrations are measured by LC−MS. MCE has not independently confirmed the accuracy of these methods. They are for reference only.**

**CUSTOMER VALIDATION**

- Cell. 2018 Sep 20;175(1):186-199.e19.
- Environ Pollut. 2021 Jan 1;268(Pt B):115748.

See more customer validations on [www.MedChemExpress.com](http://www.MedChemExpress.com)

**REFERENCES**

\textsuperscript{[1]} Blake JF, et al. Discovery of (S)-1-(1-(4-Chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one (GDC-0994), an Extracellular Signal-Regulated Kinase 1/2 (ERK1/2) Inhibitor in Early Clinical Development


\textsuperscript{[3]} MICHAEL LAI. Opportunity for Pharmaceutical Intervention in Lung Cancer: Selective Inhibition of JAK1/2 to Eliminate EMT-Derived Mesenchymal Cells.