Tomivosertib

Cat. No.: HY-100022
CAS No.: 1849590-01-7
Molecular Formula: C₁₇H₂₀N₆O₂
Molecular Weight: 340.38
Target: MNK; PD-1/PD-L1
Pathway: MAPK/ERK Pathway; Immunology/Inflammation
Storage:
- Powder: -20°C 3 years
- Powder: 4°C 2 years
- In solvent: -80°C 6 months
- In solvent: -20°C 1 month

### SOLVENT & SOLUBILITY

**In Vitro**

- **DMSO**: 4.35 mg/mL (12.78 mM; Need ultrasonic)
- **H₂O**: < 0.1 mg/mL (insoluble)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<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>2.9379 mL</td>
<td>14.6895 mL</td>
<td>29.3789 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5876 mL</td>
<td>2.9379 mL</td>
<td>5.8758 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2938 mL</td>
<td>1.4689 mL</td>
<td>2.9379 mL</td>
<td></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: ≥ 0.43 mg/mL (1.26 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   - Solubility: ≥ 0.44 mg/mL (1.29 mM); Clear solution

### BIOLOGICAL ACTIVITY

**Description**

Tomivosertib (eFT508) is a potent, highly selective, and orally bioavailable MNK1 and MNK2 inhibitor, with IC₅₀s of 1-2 nM against both isoforms. Treatment of tumor cell lines with Tomivosertib (eFT508) leads to a dose-dependent reduction in eIF4E phosphorylation at serine 209 (IC₅₀=2-16 nM)[1]. Tomivosertib (eFT508) also dramatically downregulates PD-L1 protein abundance[2].

**IC₅₀ & Target**

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>MNK1 1-2 nM (IC₅₀)</th>
<th>MNK2 1-2 nM (IC₅₀)</th>
<th>PD-L1</th>
</tr>
</thead>
</table>
In Vitro
Tomivosertib (eFT508) reduces eIF4E phosphorylation dose-dependently at serine 209 (IC\textsubscript{50}=2-16 nM) in tumor cell lines. In a panel of aprr 50 hematological cancers, Tomivosertib shows anti-proliferative activity against multiple DLBCL cell lines. Sensitivity to Tomivosertib in TMD8, OCI-Ly3 and HBL1 DLBCL cell lines is associated with dose-dependent decreases in production of pro-inflammatory cytokines including TNF\textalpha, IL-6, IL-10 and CXCL10. Further evaluation Tomivosertib mechanism of action demonstrates that decreased TNF\textalpha production correlates with a 2-fold decrease in TNF\textalpha mRNA half-life\textsuperscript{[1]}.

In Vivo
Tomivosertib (eFT508) shows significant anti-tumor activity in the TMD8 and HBL-1 ABC-DLBCL models, both of which harbor activating MyD88 mutations. Besides, Tomivosertib combines effectively with components of R-CHOP and with novel targeted agents, including PCI-32765 and Venetoclax, in human lymphoma models\textsuperscript{[3]}.

REFERENCES

\textsuperscript{[1]} Kevin R. Webster, et al. eFT508, a Potent and Selective Mitogen-Activated Protein Kinase Interacting Kinase (MNK) 1 and 2 Inhibitor, Is Efficacious in Preclinical Models of Diffuse Large B-Cell Lymphoma (DLBCL). Blood 2015 126:1554.