Lanraplenib

Cat. No.: HY-109091
CAS No.: 1800046-95-0
Molecular Formula: C₂₃H₂₅N₉O
Molecular Weight: 443.5
Target: Syk
Pathway: Protein Tyrosine Kinase/RTK
Storage:
- Powder: -20°C, 3 years; 4°C, 2 years
- In solvent: -80°C, 6 months; -20°C, 1 month

SOLVENT & SOLUBILITY

In Vitro

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Solvent</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>DMSO</td>
<td>2.2548 mL</td>
<td>11.2740 mL</td>
<td>22.5479 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>DMSO</td>
<td>0.4510 mL</td>
<td>2.2548 mL</td>
<td>4.5096 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>DMSO</td>
<td>0.2255 mL</td>
<td>1.1274 mL</td>
<td>2.2548 mL</td>
<td></td>
</tr>
</tbody>
</table>

DMSO: 41.67 mg/mL (93.96 mM; Need ultrasonic)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Solvent</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>10% DMSO</td>
<td>2.2548 mL</td>
<td>11.2740 mL</td>
<td>22.5479 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>10% DMSO</td>
<td>0.4510 mL</td>
<td>2.2548 mL</td>
<td>4.5096 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>10% DMSO</td>
<td>0.2255 mL</td>
<td>1.1274 mL</td>
<td>2.2548 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: ≥ 2.08 mg/mL (4.69 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Lanraplenib (GS-9876) is a highly selective and oral SYK inhibitor (IC₅₀=9.5 nM) in development for the treatment of inflammatory diseases. Lanraplenib (GS-9876) inhibits SYK activity in platelets via the glycoprotein VI (GPVI) receptor without prolonging bleeding time (BT) in monkeys or humans[1][2][3].

IC₅₀ & Target
IC₅₀: 9.5 nM (SYK)[1]

In Vitro
GS-9876 inhibits anti-IgM stimulated phosphorylation of Akt, BLNK, BTK, ERK, MEK, and PKCδ in human B cells with EC₅₀ values of 24-51 nM. GS-9876 inhibits anti-IgM mediated CD69 and CD86 expression on B-cells (EC₅₀=112±10 nM and 164±15 nM, respectively) and anti-IgM /anti-CD40 co-stimulated B cell proliferation (EC₅₀=108±55 nM). In
human macrophages, GS-9876 inhibits IC-stimulated TNFα and IL-1β release (EC_{50}=121±77 nM and 9±17 nM, respectively)\(^1\).

GS-9876 inhibits glycoprotein VI (GPVI)-induced phosphorylation of linker for activation of T cells and phospholipase Cγ2, platelet activation and aggregation in human whole blood, and platelet binding to collagen under arterial flow\(^2\).

REFERENCES

