Divarasib

Cat. No.: HY-145928  
CAS No.: 2417987-45-0  
Molecular Formula: C₂₉H₃₂ClF₄N₇O₂  
Molecular Weight: 622.06  
Target: Ras  
Pathway: GPCR/G Protein  
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: 100 mg/mL (160.76 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvent Concentration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 mM</td>
<td>1.6076 mL</td>
<td>8.0378 mL</td>
<td>16.0756 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3215 mL</td>
<td>1.6076 mL</td>
<td>3.2151 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1608 mL</td>
<td>0.8038 mL</td>
<td>1.6076 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 (4.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
   Solubility: 2.5 mg/mL (4.02 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil  
   Solubility: ≥ 2.5 mg/mL (4.02 mM); Clear solution

BIOLOGICAL ACTIVITY

Description  
Divarasib (GDC-6036) is an orally bioavailable, highly potent, and selective KRAS G12C inhibitor with an IC₅₀ of <0.01 μM. Divarasib covalently binds to the switch II (SW-II) pocket of KRAS G12C and irreversibly locks it in the inactive GDP-bound state.

IC₅₀ & Target  
K-Ras(G12C)  
<0.01 μM (IC₅₀)
In Vitro

Divarasib (compound 17a) has an EC$_{50}$ of 2 nM in K-Ras G12C-alkylation HCC1171 cells$^{[2]}$
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Divarasib (10-100 mg/kg/day; PO for 7 days) decreases the ratio of free KRAS G12C$^{[1]}$.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

<table>
<thead>
<tr>
<th>Animal Model:</th>
<th>Female C.B-17 SCID (Inbred) mice (20-21 weeks old; 24.1 g) with human NSCLC NCI-H2030.X1.1 cells$^{[1]}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage:</td>
<td>10, 25, or 100 mg/kg</td>
</tr>
<tr>
<td>Administration:</td>
<td>Oral gavage (PO) every day (QD) for 7 days (vehicle: 0.5% methylcellulose)</td>
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<tr>
<td>Result:</td>
<td>Decreased the ratio of free KRAS G12C to internal standard. Dose-dependent target engagement was observed for all time points (2, 8, and 24 h post-last dose), with over 90% KRAS G12C engagement observed for the highest dose 100 mg/kg assessed.</td>
</tr>
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</table>

REFERENCES
