INCB-057643

Cat. No.: HY-111485
CAS No.: 1820889-23-3
Molecular Formula: C₂₀H₂₁N₃O₅S
Molecular Weight: 415.46
Target: Epigenetic Reader Domain; Apoptosis
Pathway: Epigenetics; Apoptosis
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 : 62.5 mg/mL (150.44 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing</th>
<th>Concentration</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>1 mM</td>
<td>2.4070 mL</td>
<td>12.0349 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4814 mL</td>
<td>2.4070 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2407 mL</td>
<td>1.2035 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: ≥ 2.08 mg/mL (5.01 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.01 mM); Clear solution

3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.01 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

INCB-057643 is a novel, orally bioavailable BET inhibitor.

IC₅₀ & Target

BET

In Vitro

INCB-057643 is a novel, orally bioavailable BET inhibitor. INCB-057643 inhibits binding of BRD2/BRD3/BRD4 to an acetylated histone H4 peptide in the low nM range, and is selective against other bromodomain containing proteins.
In vitro analyses show that INCB-057643 inhibits proliferation of human AML, DLBCL, and multiple myeloma cell lines, with a corresponding decrease in MYC protein levels. Cell cycle analyses indicate that G₁ arrest and a concentration-dependent increase in apoptosis are seen within 48 hours of treatment with INCB-057643[1].

| In Vivo | Production of several cytokines, including IL-6, IL-10 and MIP-1α, is repressed by INCB-057643 in human and mouse whole blood stimulated ex vivo with LPS. Oral administration of INCB-057643 results in significant anti-tumor efficacy in xenograft models of AML, myeloma, and DLBCL. Additionally, combining INCB-057643 with standard of care agents used for the treatment of DLBCL including rituximab and bendamustine results in enhanced anti-tumor efficacy relative to that achieved with single agent therapies at doses that are well tolerated[1]. |

REFERENCES