VTP50469

Cat. No.: HY-114162
CAS No.: 2169916-18-9
Molecular Formula: C₃₂H₄₇FN₆O₄S
Molecular Weight: 630.82
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 : 125 mg/mL (198.15 mM; Need ultrasonic)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>1.5852 mL</td>
<td>7.9262 mL</td>
<td>15.8524 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3170 mL</td>
<td>1.5852 mL</td>
<td>3.1705 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1585 mL</td>
<td>0.7926 mL</td>
<td>1.5852 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 (3.30 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 2.08 mg/mL (3.30 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.08 mg/mL (3.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
VTP50469 is a potent, highly selective and orally active **Menin-MLL interaction** inhibitor with a \( K_i \) of 104 pM.
VTP50469 has potently anti-leukemia activity\(^1\)\(^2\).

IC\(_{50}\) & Target
Ki: 104 pM (Menin-MLL interaction)\(^1\)\(^2\)

In Vitro
VTP50469 more potently and rapidly inhibits cell proliferation in a concentration-dependent manner in MLL-r cell
lines carrying (MOLM13 (IC_{50} of 13 nM), THP1 (IC_{50} of 37 nM), NOMO1 (IC_{50} of 30 nM), ML2 (IC_{50} of 16 nM), EOL1 (IC_{50} of 20 nM), and murine MLL-AF9 cells (IC_{50} of 15 nM)) and ALL (KOPN8 (IC_{50} of 15 nM), HB11;19 (IC_{50} of 36 nM), MV4;11 (IC_{50} of 17 nM), SEMK2 (IC_{50} of 27 nM), and RS4;11 (IC_{50} of 25 nM)) cell lines\[1\].

At early timepoints MLL-r B cell ALL (B-ALL) cell lines, but not MLL-r AML cell lines, underwent apoptosis in response to VTP50469 in a dose-dependent manner. MLL-r AML cell lines underwent dose-dependent differentiation starting at 4-6 days of exposure to VTP50469\[1\].

VTP50469 displaces Menin from protein complexes and inhibits chromatin occupancy of MLL at select genes. Loss of MLL binding led to changes in gene expression, differentiation, and apoptosis\[1\].

**In Vivo**

VTP50469 (15-60 mg/kg; oral administration; twice a day; for 28 days; NSG mice) treatment is highly efficacious across all dosage levels and all treatment groups have a significant survival advantage. Mice dosed at 30 and 60 mg/kg VTP50469 extends survival advantage\[1\].

<table>
<thead>
<tr>
<th>Animal Model:</th>
<th>Unconditioned immunodeficient (NSG) mice with MV4;11 cells[1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage:</td>
<td>15 mg/kg, 30 mg/kg, and 60 mg/kg</td>
</tr>
<tr>
<td>Administration:</td>
<td>Oral administration; twice a day; for 28 days</td>
</tr>
<tr>
<td>Result:</td>
<td>Was highly efficacious across all dosage levels and all treatment groups had a significant survival advantage over the control group.</td>
</tr>
</tbody>
</table>

**REFERENCES**
