IPN60090

Cat. No.: HY-103671
CAS No.: 1853164-83-6
Molecular Formula: C₂₄H₂₇F₃N₈O₃
Molecular Weight: 532.52
Target: Glutaminase
Pathway: Metabolic Enzyme/Protease
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 : 31.43 mg/mL (59.02 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent 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>1.8779 mL</td>
<td>9.3893 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3756 mL</td>
<td>1.8779 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1878 mL</td>
<td>0.9389 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 >> 90% corn oil
Solubility: ≥ 3.14 mg/mL (5.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
IPN-60090 is an orally active and highly selective inhibitor of glutaminase 1 (GLS1; IC₅₀=31 nM), with no activity observed against GLS-2. IPN-60090 exhibits excellent physicochemical and pharmacokinetic properties in vivo. IPN-60090 can be used for solid tumors research, such as lung and ovarian cancers[1][2].

IC₅₀ & Target
IC₅₀: 31 nM (GLS1)[2]

In Vitro
There are two known isoforms of glutaminase: GLS-1 (also called kidney-type or KGA), and GLS-2 (also called liver-type or LGA). GLS-1 is ubiquitous and GLS-2 expression appears limited primarily to the liver.
In a dual-coupled enzyme assay, IPN60090 inhibits purified recombinant human GLS-1 (GAC isoform) with an IC₅₀ of 31 nM, and has no activity against GLS-2, with an IC₅₀ of >50000 nM[2].
IPN60090 inhibits the proliferation of A549 cells with an IC₅₀ of 26 nM[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo

IPN60090 (3 mg/kg for i.v.; 10 mg/kg for p.o.) has excellent pharmacokinetic properties, with CL=4.1 mL/min/kg, t$_{1/2}$=1 hour, $C_{\text{max}}$=19 μM, F%=89%$^{[2]}$.

IPN-60090 (oral administration; 100 mg/kg; twice daily; 30 days) shows similar efficacy and target engagement to CB-839 (HY-12248) dosed orally at 250 mg/kg twice daily. And the 100 mg/kg BID dose of IPN-60090 is a tolerated dose for the following model study$^{[2]}$.

IPN-60090 (oral administration; 100 mg/kg; twice daily; 30 days; monotherapy or in combination with TAK228 (HY-13328)) causes tumor growth inhibition. IPN-60090 alone demonstrates robust in vivo target engagement in a dose-dependent manner. The glutamate/glutamine ratios and the free plasma concentrations of IPN-60090 at 4 hours post-dose on both day 4 and day 28 are all decreased$^{[2]}$. Furthermore, IPN-60090 in combination with TAK228 strongly causes an 85% tumor growth inhibition, IPN-60090 alone causes a 28% tumor growth inhibition in vivo$^{[2]}$.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

<table>
<thead>
<tr>
<th>Animal Model:</th>
<th>Female CD-1 mice$^{[2]}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage:</td>
<td>3 mg/kg for i.v.; 10 mg/kg for p.o. (Pharmacokinetic Analysis)</td>
</tr>
<tr>
<td>Administration:</td>
<td>Intravenous injection and oral administration</td>
</tr>
<tr>
<td>Result:</td>
<td>CL (4.1 mL/min/kg), t$<em>{1/2}$ (1 hour) for i.v.; $C</em>{\text{max}}$ (19 μM), F% (89%) for p.o..</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Animal Model:</th>
<th>Ru337 non-small cell lung cancer patient-derived xenograft (PDX) subcutaneous mouse model as monotherapy or in combination$^{[2]}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage:</td>
<td>100 mg/kg</td>
</tr>
<tr>
<td>Administration:</td>
<td>Oral administration; 100 mg/kg; twice daily; 30 days; monotherapy or in combination with TAK228</td>
</tr>
<tr>
<td>Result:</td>
<td>Exhibited an improvement in the combination regimen group over either single agent.</td>
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REFERENCES
