Luminespib

Cat. No.: HY-10215
CAS No.: 747412-49-3
Molecular Formula: C₂₆H₃₁N₃O₅
Molecular Weight: 465.54
Target: HSP; Autophagy
Pathway: Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Autophagy
Storage: Powder -20°C 3 years
4°C 2 years
In solvent -80°C 6 months
-20°C 1 month

Solvent & Solubility

<table>
<thead>
<tr>
<th>In Vitro</th>
<th>DMSO: ≥ 62 mg/mL (133.18 mM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>*“≥” means soluble, but saturation unknown.</td>
</tr>
</tbody>
</table>

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.1480 mL</td>
<td>10.7402 mL</td>
<td>21.4804 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.4296 mL</td>
<td>2.1480 mL</td>
<td>4.2961 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2148 mL</td>
<td>1.0740 mL</td>
<td>2.1480 mL</td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

BIOLICAL ACTIVITY

Description

NVP-AUY922 is a potent HSP90 inhibitor with IC₅₀'s of 7.8 and 21 nM for HSP90α and HSP90β, respectively.

IC₅₀ & Target

<table>
<thead>
<tr>
<th>HSP90α</th>
<th>HSP90β</th>
<th>GRP94</th>
<th>TRAP-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.8 nM (IC₅₀)</td>
<td>21 nM (IC₅₀)</td>
<td>535 nM (IC₅₀)</td>
<td>85 nM (IC₅₀)</td>
</tr>
</tbody>
</table>

In Vitro

NVP-AUY922 is a potent and selective HSP90 inhibitor, with IC₅₀'s and Kᵢ's of 21 ± 16, 8.2 ± 0.7 nM against HSP90β and of 7.8 ± 1.8, 9.0 ± 5.0 nM for HSP90α. NVP-AUY922 shows weak activity against GRP94 and TRAP-1 with IC₅₀'s of 535 ± 51 nM (Kᵢ, 108 nM) and 85 ± 8 nM (Kᵢ, 53 nM), respectively. NVP-AUY922 exhibits inhibitory effect on proliferation of various human tumor cell lines (2.3–49.6 nM), induces cell cycle arrest and apoptosis and depletes client proteins in human cancer cells (80 nM) [1]. NVP-AUY922 (100 nM) significantly reduces CD40L fibroblast-induced changes in immunophenotype and STAT3 signaling but with no effect on the viability of chronic lymphocytic leukemia (CLL) cells. NVP-AUY922 (500 nM) in combination with fludarabine more effectively induces apoptosis in cells in co-culture than either drug alone, and overcomes fibroblast-derived resistance to Hsp90 inhibitor [2]. NVP-
AY922 shows great inhibition of pancreatic cancer cells with IC_{50} of at 10 nM. NVP-AUY922 (10 nM) reduces the expression and the epidermal growth factor (EGF)-mediated activation of EGFR and substantially disrupts EGF signaling in terms of diminishing downstream phosphorylation of ERK\textsubscript{Thr202/Tyr204}. NVP-AUY922 (10 nM) significantly blocks pancreatic cancer cell migration and invasion both in the absence and presence of EGF\textsuperscript{[3]}.

<table>
<thead>
<tr>
<th>In Vivo</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVP-AUY922 (50, 75 mg/kg, i.p.) significantly inhibits tumor growth rate, reducing the mean weights of tumors on day 11 in human tumor xenografts\textsuperscript{[2]}. NVP-AUY922 (50 mg/kg/week, 3\times25 mg/kg/week) significantly reduces tumor growth rates and lowers tumor weights in the L3.6pl pancreatic cancer cell-bearing mice model\textsuperscript{[3]}.</td>
</tr>
</tbody>
</table>

**PROTOCOL**

**Cell Assay \textsuperscript{[1]}**

Cell lines are grown in DMEM/10% FCS, 2 mM glutamine, and nonessential amino acids in a humidified atmosphere of 5% CO\textsubscript{2} in air. All lines are free of Mycoplasma. Cell proliferation is determined using the SRB assay for tumor cells and prostate epithelial cells, the WST-1 assay for MCF10A and HB119, or an alkaline phosphatase assay for HUVEC and HDMEC. GI\textsubscript{50} is the compound concentration inhibiting cell proliferation by 50% compared with vehicle controls. Active caspase-3/7 is measured using a homogenous caspase assay kit\textsuperscript{[1]}.

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

**Animal Administration \textsuperscript{[1]}**

Mice\textsuperscript{[1]}

For efficacy studies, human tumor xenografts are established s.c. in athymic mice. WM266.4 cells are also injected i.v. to generate experimental lung metastases and PC3LN3 prostate carcinoma cells are implanted into the prostates of male mice. Dosing by i.p. with NVP-AUY922 commences when tumors are well established. Tumor growth is monitored and at study end samples are harvested for analysis\textsuperscript{[1]}.

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

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**REFERENCES**


