XL228

Cat. No.: HY-15749
CAS No.: 898280-07-4
Molecular Formula: C₂₂H₃₁N₉O
Molecular Weight: 437.54
Target: Aurora Kinase; Bcr-Abl; IGF-1R; Src
Pathway: Cell Cycle/DNA Damage; Epigenetics; Protein Tyrosine Kinase/RTK
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 : ≥ 83.33 mg/mL (190.45 mM)
* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td></td>
<td>2.2855 mL</td>
<td>11.4275 mL</td>
<td>22.8551 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.4571 mL</td>
<td>2.2855 mL</td>
<td>4.5710 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.2286 mL</td>
<td>1.1428 mL</td>
<td>2.2855 mL</td>
</tr>
</tbody>
</table>

Preparing Stock Solutions

In Vivo

1. Add each solvent one by one:  10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.75 mM); Clear solution
2. Add each solvent one by one:  10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.75 mM); Clear solution
3. Add each solvent one by one:  10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
XL228 is a multi-targeted tyrosine kinase inhibitor with IC₅₀s of 5, 3.1, 1.6, 6.1, 2 nM for Bcr-Abl, Aurora A, IGF-1R, Src and Lyn, respectively.

IC₅₀ & Target

<table>
<thead>
<tr>
<th>Aurora A</th>
<th>IGF-1R</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 nM (IC₅₀)</td>
<td>1.6 nM (IC₅₀)</td>
</tr>
</tbody>
</table>
In Vitro

XL228 shows a broad pattern of protein kinase inhibition, including the tyrosine kinases IGF1R, SRC, ABL, FGFR1-3, and ALK and the serine/threonine kinases Aurora A and Aurora B. A panel of kinase inhibitors including XL228 is profiled against a series of cancer cell lines with known alterations in major signaling pathways. Approximately 30% of the lines demonstrate XL228 IC50 values of <100nM in viability assays, including many lines with characterized ALK or FGFR mutations or amplifications. XL228 eliminates the phosphorylation of Aurora A and B at concentrations above 10 nM. Short-term treatment of HeLa cells leads to disruption of mitotic spindle formation, with the majority of mitotic cells exhibiting a unipolar spindle and disorganized chromosomes[2]. It displays low nanomolar biochemical activity against wild type Abl kinase (K_i=5 nM), as well as the T315I form of Abl resistant to imatinib and dasatinib (K_i=1.4 nM). XL228 inhibits phosphorylation of BCR-ABL and its substrate STAT5 in K562 cells in vitro with IC50s of 33 and 43 nM, respectively[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Single-dose pharmacodynamics studies demonstrate a potent effect of XL228 on BCR-ABL signaling in K562 xenograft tumors. Phosphorylation of BCR-ABL is decreased by 50% at XL228 plasma concentrations of 3.5 μM; a similar decrease in phospho-STAT5 occurred at 0.8 μM plasma concentration[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Customer Validation

- Science. 2017 Dec 1;358(6367):eaan4368.
- Technical University of Munich. 24.01.2018.

See more customer validations on www.MedChemExpress.com

References

