**KW-2449**

**Cat. No.:** HY-10339  
**CAS No.:** 1000669-72-6  
**Molecular Formula:** C₂₀H₂₀N₄O  
**Molecular Weight:** 332.4  
**Target:** FLT3; FGFR; Bcr-Abl; Aurora Kinase; Apoptosis  
**Pathway:** Protein Tyrosine Kinase/RTK; Cell Cycle/DNA Damage; 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 : ≥ 50 mg/mL (150.42 mM)  
* "≥" means soluble, but saturation unknown.  

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<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>3.0084 mL</td>
<td>15.0421 mL</td>
<td>30.0842 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.6017 mL</td>
<td>3.0084 mL</td>
<td>6.0168 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3008 mL</td>
<td>1.5042 mL</td>
<td>3.0084 mL</td>
<td></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: ≥ 2.5 mg/mL (7.52 mM); Clear solution  
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (7.52 mM); Clear solution  
3. Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (7.52 mM); Clear solution

**BIOLOGICAL ACTIVITY**

**Description**  
KW-2449 is a multi-targeted kinase inhibitor of FLT3, ABL, ABL\(^{T315I}\) and Aurora kinase with IC\(_{50}\)s of 6.6, 14, 4 and 48 nM, respectively.

<table>
<thead>
<tr>
<th>IC(_{50}) &amp; Target</th>
<th>Abl</th>
<th>ABL-T315I</th>
<th>FGFR1</th>
<th>Aurora A</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 nM (IC(_{50}))</td>
<td>14 nM (IC(_{50}))</td>
<td>36 nM (IC(_{50}))</td>
<td>48 nM (IC(_{50}))</td>
<td></td>
</tr>
</tbody>
</table>
**In Vitro**
KW-2449 shows growth inhibitory activities against FLT3/ITD-, FLT3/D835Y-, and wt-FLT3/FL-expressing 32D cells, MOLM-13 and MV4;11 with GI\(50\) values of 0.024, 0.046, 0.014, 0.024, and 0.011 \(\mu M\), respectively. KW-2449 suppresses the phosphorylations of FLT3 (P-FLT3) and its downstream molecule phospho-STAT5 (P-STAT5) in MOLM-13 cells in a dose-dependent manner. KW-2449 increases the percentage of cells in the G1 phase of the cell cycle and reciprocally reduced the percentage of cells in the S phase, resulting in the increase of apoptotic cell population\(^1\).

**In Vivo**
Oral administration of KW-2449 shows dose-dependent and significant tumor growth inhibition in FLT3-mutated xenograft model with minimum bone marrow suppression. In FLT3 wild-type human leukemia, it induces the reduction of phosphorylated histone H3, G2/M arrest, and apoptosis. In imatinib-resistant leukemia, KW-2449 contributes to release of the resistance by the simultaneous down-regulation of BCR/ABL and Aurora kinases. Furthermore, the antiproliferative activity of KW-2449 is confirmed in primary samples from AML and imatinib-resistant patients. The inhibitory activity of KW-2449 is not affected by the presence of human plasma protein, such as \(\alpha1\)-acid glycoprotein\(^1\).

**PROTOCOL**

| Cell Assay \(^1\) | Cell viability is determined by the sodium 3′-[1-(phenylaminocarbonyl)-3, 4-tetrazolium]-bis (4-methoxy-6-nitro) benzene sulfonic acid hydrate assay after incubation with or without KW-2449 for 72 hours at 37°C. The number of viable cells is determined using the Cell Proliferation Kit II\(^1\). MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

| Animal Administration \(^1\) | Mice: SCID mice are subcutaneously inoculated with MOLM-13 cells. Five days after inoculation, tumor volume is measured using the Antitumor test system II. The 25 mice with tumors ranging from 90 to 130 \(mm^3\) are selected and randomized using the Antitumor test system II. From the day of randomization, vehicle (0.5 wt/vol% MC400) or KW-2449 (2.5, 5.0, 10, and 20 mg/kg) is orally administered to mice twice a day for 14 days. Tumor volume is measured twice a week during the treatment\(^1\). MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

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**REFERENCES**
