**KU-0060648**

Cat. No.: HY-13431  
CAS No.: 881375-00-4  
Molecular Formula: C₃₃H₃₄N₄O₄S  
Molecular Weight: 582.71  
Target: DNA-PK; PI3K; mTOR  
Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR  
Storage: Please store the product under the recommended conditions in the COA.

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**BIOLOGICAL ACTIVITY**

**Description**  
KU-0060648 is a dual inhibitor of PI3K and DNA-PK with IC₅₀ values of 4 nM, 0.5 nM, 0.1 nM, 0.594 nM and 8.6 nM for PI3Kα, PI3Kβ, PI3Kγ, PI3Kδ and DNA-PK, respectively[1].

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>PI3Kα 4 nM (IC₅₀)</th>
<th>PI3Kβ 0.5 nM (IC₅₀)</th>
<th>PI3Kγ 0.594 μM (IC₅₀)</th>
<th>PI3Kδ 0.1 nM (IC₅₀)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA-PK</td>
<td>8.6 nM (IC₅₀)</td>
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</tbody>
</table>

**In Vitro**  
KU-0060648 inhibits cellular DNA-PK auto-phosphorylation with IC₅₀ values of 0.019 μM (MCF7 cells) and 0.17 μM (SW620 cells), and PI-3K-mediated AKT phosphorylation with IC₅₀ values of 0.039 μM (MCF7 cells) and >10 μM (SW620 cells)[1].  
KU-0060648 (30-500 nM; 72 hours) dose-dependently inhibits HepG2 cell proliferation, IC₅₀=134.32nM[2].  
KU-0060648 (0.1-1 μM; 5 days) inhibits cell lines growth with IC₅₀ values of 0.95 μM, 0.21 μM, 0.27 μM, 0.41 μM and 1 μM in SW620, LoVo, MCF7, T47D and MDA-MB-231 cells[1].  
KU-0060648 (100-300 nM; 12 hours) significantly inhibits activation of PI3K (p85 phosphorylation), AKT (Ser-473 and Thr-308 phosphorylations) and mTOR (p70S6K1 Thr-389 phosphorylation) in HepG2/Huh-7 lines and primary human HCC cells[2].

**Cell Proliferation Assay[1]**

<table>
<thead>
<tr>
<th>Cell Line:</th>
<th>Human breast (MCF7, T47D and MDA-MB-231) and colon (LoVo and SW620) cancer cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration:</td>
<td>0.1-1 μM</td>
</tr>
<tr>
<td>Incubation Time:</td>
<td>5 days</td>
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<td>Result:</td>
<td>Resulted in &gt; 50% inhibition of cell growth in all cell lines.</td>
</tr>
</tbody>
</table>

**Western Blot Analysis[2]**

| Cell Line: | HCC cells; HepG2/Huh-7 cells |

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Concentration: 100-300 nM
Incubation Time: 12 hours
Result: Inhibited phosphatidylinositol 3-kinase (PI3K) and in-activates AKT-mTOR signaling.

In Vivo
KU-0060648 (intraperitoneal injection; 10 and 50 mg/kg; once daily; daily for 21 days) dramatically inhibits HepG2 xenograft growth in nude mice, the tumor weights (at week 5) of KU-0060648 group mice are dramatically lighter than that of vehicle control mice and exert a dose-dependent effect in vivo[1].

Animal Model: HepG2 xenograft nude mice model[1]
Dosage: 10 and 50 mg/kg
Administration: Intraperitoneal injection; 10 and 50 mg/kg; once daily; daily for 21 days
Result: Suppressed HepG2 xenograft growth in nude mice.

REFERENCES