LY2835219

Cat. No.: HY-16297
CAS No.: 1231930-82-7
Molecular Formula: C₂₈H₃₆F₂N₈O₃S
Molecular Weight: 602.7
Target: CDK
Pathway: Cell Cycle/DNA Damage
Storage:
- Powder
  -20°C 3 years
  4°C 2 years
- In solvent
  -80°C 6 months
  -20°C 1 month

Solvent & Solubility

In Vitro

H₂O : ≥ 250 mg/mL (414.80 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></td>
<td>1 mM</td>
<td>1.6592 mL</td>
<td>8.2960 mL</td>
<td>16.5920 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.3318 mL</td>
<td>1.6592 mL</td>
<td>3.3184 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.1659 mL</td>
<td>0.8296 mL</td>
<td>1.6592 mL</td>
</tr>
</tbody>
</table>

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

In Vivo

1. LY2835219 is dissolved in 1% HEC in 20 mM phosphate buffer (pH 2.0) and administered orally by gavage (final volume 0.2 mL)[4].

BIOLOGICAL ACTIVITY

Description
LY2835219 a selective CDK4/6 inhibitor with IC₅₀s of 2 nM and 10 nM for CDK4 and CDK6, respectively.

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>Cdk4/cyclin D1 2 nM (IC₅₀)</th>
<th>CDK6/cyclinD1 10 nM (IC₅₀)</th>
<th>CDK9/cyclinT1 57 nM (IC₅₀)</th>
<th>CDK5/p35 287 nM (IC₅₀)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cdk5/p25 355 nM (IC₅₀)</td>
<td>CDK2/cyclinE 504 nM (IC₅₀)</td>
<td>CDK1/cyclinB1 1627 nM (IC₅₀)</td>
<td>CDK7/Mat1/cyclinH1 3910 nM (IC₅₀)</td>
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<td></td>
<td>PIM1 50 nM (IC₅₀)</td>
<td>PIM2 3400 nM (IC₅₀)</td>
<td>HIPK2 31 nM (IC₅₀)</td>
<td>DYRK2 61 nM (IC₅₀)</td>
</tr>
<tr>
<td>Target</td>
<td>IC&lt;sub&gt;50&lt;/sub&gt;</td>
<td></td>
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<tr>
<td>------------------------</td>
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<tr>
<td>CK2</td>
<td>117 nM (IC&lt;sub&gt;50&lt;/sub&gt;)</td>
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<tr>
<td>GSK3b</td>
<td>192 nM (IC&lt;sub&gt;50&lt;/sub&gt;)</td>
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<tr>
<td>JNK3</td>
<td>389 nM (IC&lt;sub&gt;50&lt;/sub&gt;)</td>
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<tr>
<td>FLT3 (D835Y)</td>
<td>403 nM (IC&lt;sub&gt;50&lt;/sub&gt;)</td>
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<tr>
<td>DRAK1</td>
<td>659 nM (IC&lt;sub&gt;50&lt;/sub&gt;)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>FLT3</td>
<td>3960 nM (IC&lt;sub&gt;50&lt;/sub&gt;)</td>
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</table>

**In Vitro**

LY2835219 reduces cell viability with the IC<sub>50</sub> values ranging from 0.5 μM to 0.7 μM, inhibits Akt and ERK signaling but not mTOR activation at head and neck squamous cell carcinoma (HNSCC) cells<sup>[1]</sup>. LY2835219 shows inhibition on A375R1-4, M14R, and SH4R with EC<sub>50</sub> values ranging from 0.3 to 0.6 μM; LY2835219 inhibits the proliferation of the parental A375 and resistant A375RV1 and A375RV2 cells with similar potencies with IC<sub>50</sub> values of 395, 260, and 463 nM, respectively<sup>[2]</sup>. LY2835219 inhibits CDK4 and CDK6 with low nanomolar potency, inhibits Rb phosphorylation resulting in a G1 arrest and inhibition of proliferation, and its activity is specific for Rb-proficient cells<sup>[3]</sup>.

**In Vivo**

LY2835219 (45 mg/kg, p.o.) in combination with everolimus causes a cooperative antitumor effect in HNSCC xenograft tumor<sup>[1]</sup>. LY2835219 (45 or 90 mg/kg, p.o.) shows significant tumor growth inhibition in an A375 xenograft model<sup>[2]</sup>.

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**PROTOCOL**

**Kinase Assay**<sup>[1]</sup>

Cells (5 × 10<sup>3</sup>) are plated in 96 well plates. Cells are treated the next day for 24 to 48 hours and then assessed for caspase-3 activity by Caspase-Glo-3/7 Assay, as per manufacturer’s instructions and a luminescence plate reader. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**Cell Assay**<sup>[1]</sup>

Cells are seeded in a 96-well plate, allowed to adhere overnight, and treated with DMSO control (0.1% v/v) or the indicated compounds for 72 h. Cell viability and proliferation are determined using a Cell Counting Kit according to the manufacturer’s instructions. The interaction between LY2835219 and mTOR inhibitor is determined using CompuSyn. Combination index (CI) values of 1 indicates and additive drug interaction, whereas a CI of < 1 is synergistic and a CI of > 1 is antagonistic.

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

**Animal Administration**<sup>[1]</sup>

Six-week-old BALB/c female nude mice are injected subcutaneously with OSC-19 (1×10<sup>6</sup>) cells. When tumor sizes reach approximately 100 mm<sup>3</sup>, mice are randomized by tumor size and subjected to each treatment. At least 5 mice per treatment group are included. Each group of mice is dosed via daily oral gavage with vehicle, LY2835219 (45 mg/kg/d or 90 mg/kg/d), Everolimus (5 mg/kg/d), or a combination of both. The LY2835219 is dissolved in 1% HEC in 20 mM phosphate buffer (pH2.0). Tumor size and body weight are measured twice weekly. Tumor volumes are calculated using the following formula: V=(L × W<sup>2</sup>)<sup>/2</sup> (L, Length; W, width). Mice are gavaged a final time on day 14 and sacrificed the following day. The tumors are removed for Western blot and immunohistochemistry.

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

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**CUSTOMER VALIDATION**

- *Cancer Res*. 2017 May 1;77(9):2488-2499.
REFERENCES


