**Milciclib**

Cat. No.: HY-10424  
CAS No.: 802539-81-7  
Molecular Formula: C₂₅H₃₂N₈O  
Molecular Weight: 460.57  
Target: CDK; Autophagy  
Pathway: Cell Cycle/DNA Damage; Autophagy  
Storage: Powder -20°C 3 years; 4°C 2 years; In solvent -80°C 6 months; -20°C 1 month

**SOLVENT & SOLUBILITY**

**In Vitro**

<table>
<thead>
<tr>
<th>Solvent &amp; Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO 20 mg/mL (43.42 mM)</td>
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</tbody>
</table>

**Preparing Stock Solutions**

- 1 mM: 2.1712 mL  
- 5 mM: 0.4342 mL  
- 10 mM: 0.2171 mL

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 mg/mL (4.34 mM); Clear solution  
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
   Solubility: ≥ 2 mg/mL (4.34 mM); Clear solution

**BIOLOGICAL ACTIVITY**

**Description**

Milciclib (PHA-848125) is a potent, dual inhibitor of CDK and Tropomyosin receptor kinase (TRK), with IC₅₀ values of 45, 150, 160, 363, 398 nM and 53 nM for cyclin A/CDK2, cyclin H/CDK7, cyclin D1/CDK4, cyclin E/CDK2, cyclin B/CDK1 and TRKA, respectively.

**IC₅₀ & Target**

<table>
<thead>
<tr>
<th>Target</th>
<th>IC₅₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclin A/CDK2</td>
<td>45 nM (IC₅₀)</td>
</tr>
<tr>
<td>cyclin E/CDK2</td>
<td>363 nM (IC₅₀)</td>
</tr>
<tr>
<td>cyclin H/CDK7</td>
<td>150 nM (IC₅₀)</td>
</tr>
<tr>
<td>cyclin D1/CDK4</td>
<td>160 nM (IC₅₀)</td>
</tr>
<tr>
<td>cyclin B/CDK1</td>
<td>398 nM (IC₅₀)</td>
</tr>
<tr>
<td>TRKA</td>
<td>53 nM (IC₅₀)</td>
</tr>
</tbody>
</table>
### In Vitro
Milciclib (PHA-848125; 0.156 or 0.625 μM) up-regulates the expression of PDCD4, DDIT4, SESN2/sestrin 2 and DEPDC6/DEPTOR in GL-Mel cells\(^1\). Milciclib (PHA-848125) potently inhibits the kinase activity of CDK2/cyclin A complex and of TRKA in a biochemical assay, with IC\(_{50}\)s of 45 and 53 nM, respectively. Milciclib induces a clear accumulation of cells in G1 phase. Milciclib strongly inhibits NGF-induced phosphorylation of TRKA in a dose-dependent manner\(^2\).

### In Vivo
Milciclib (PHA-848125; 5, 10, and 15 mg/kg, p.o.) inhibits the growth of tumor in 7,12-dimethylbenz(a)anthracene (DMBA)-induced rat mammary carcinoma model. Milciclib has significant antitumor activity in various human xenografts and carcinogen-induced tumors as well as in disseminated primary leukemia models, with plasma concentrations in rodents in the same range as those found active in inhibiting cancer cell proliferation\(^2\). Milciclib (PHA-848125; 40 mg/kg) induces a significant tumor growth inhibition in K-Ras\(^{G12D}\) LA2 mice, and this is accompanied by a reduction in the cell membrane turnover\(^3\).

### PROTOCOL

#### Cell Assay \(^2\)
Cells are seeded into 96- or 384-well plates at densities ranging from 10,000 to 30,000/cm\(^2\) in appropriate medium plus 10% FCS. After 24 hours, cells are treated in duplicate with serial dilutions of Milciclib, and 72 hours later, viable cell number is assessed using the CellTiter-Glo Assay. IC\(_{50}\)s are calculated using a Sigmoidal fitting algorithm. Experiments are done independently at least twice.

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

#### Animal Administration \(^2\)
Rats are randomized and introduced into the study when at least one mammary tumor attained a diameter of 0.5 cm. Groups of 10 animals are treated orally twice a day continuously for 10 days with vehicle (glucosate) or with 5, 10, and 15 mg/kg of Milciclib, whereas a further group receives two cycles of Milciclib at 20 mg/kg orally twice a day for 5 days with an intervening rest period of 1 week. Tumor volume is measured regularly by caliper for the duration of the experiment.

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

### CUSTOMER VALIDATION
- Technical University of Munich. 24.01.2018.

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### REFERENCES
Caution: Product has not been fully validated for medical applications. For research use only.

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