**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**  
DMSO : 20 mg/mL (43.42 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvent Concentration</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1 mM</td>
<td>2.1712 mL</td>
<td>10.8561 mL</td>
<td>21.7122 mL</td>
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</tr>
<tr>
<td>5 mM</td>
<td>0.4342 mL</td>
<td>2.1712 mL</td>
<td>4.3424 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2171 mL</td>
<td>1.0856 mL</td>
<td>2.1712 mL</td>
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</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 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 IC₅₀s 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.

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
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<tbody>
<tr>
<td>cyclin A/CDK2</td>
</tr>
<tr>
<td>cyclin E/CDK2</td>
</tr>
<tr>
<td>cyclin H/CDK7</td>
</tr>
<tr>
<td>cyclin D1/CDK4</td>
</tr>
<tr>
<td>cyclin B/CDK1</td>
</tr>
<tr>
<td>TRKA</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. 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.

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

**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. 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.

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**PROTOCOL**

**Cell Assay**

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.

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**Animal Administration**

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 (glucose) 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.

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**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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