### Milciclib

**Cat. No.:** HY-10424  
**CAS No.:** 802539-81-7  
**Molecular Formula:** C_{25}H_{32}N_{8}O  
**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>Solvent</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparing Stock Solutions</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>
<td></td>
</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>
<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 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 IC_{50}s 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.

#### IC_{50} & Target

<table>
<thead>
<tr>
<th>cyclin A/CDK2 45 nM (IC_{50})</th>
<th>cyclin E/CDK2 363 nM (IC_{50})</th>
<th>cyclin H/CDK7 150 nM (IC_{50})</th>
<th>cyclin D1/CDK4 160 nM (IC_{50})</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclin B/CDK1 398 nM (IC_{50})</td>
<td>TRKA 53 nM (IC_{50})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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| **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


