Veliparib

<table>
<thead>
<tr>
<th>Cat. No.:</th>
<th>HY-10129</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS No.:</td>
<td>912444-00-9</td>
</tr>
<tr>
<td>Molecular Formula:</td>
<td>C₁₃H₁₆N₄O</td>
</tr>
<tr>
<td>Molecular Weight:</td>
<td>244.29</td>
</tr>
<tr>
<td>Target:</td>
<td>PARP; Autophagy</td>
</tr>
<tr>
<td>Pathway:</td>
<td>Cell Cycle/DNA Damage; Epigenetics; Autophagy</td>
</tr>
<tr>
<td>Storage:</td>
<td>Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month</td>
</tr>
</tbody>
</table>

**SOLVENT & SOLUBILITY**

**In Vitro**

DMSO: ≥ 29 mg/mL (118.71 mM)

* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass of 1 mg</th>
<th>Mass of 5 mg</th>
<th>Mass of 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>4.0935 mL</td>
<td>20.4675 mL</td>
<td>40.9350 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.8187 mL</td>
<td>4.0935 mL</td>
<td>8.1870 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.4093 mL</td>
<td>2.0467 mL</td>
<td>4.0935 mL</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: ≥ 2.5 mg/mL (10.23 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (10.23 mM); Clear solution

3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (10.23 mM); Clear solution

**BIOLOGICAL ACTIVITY**

**Description**

Veliparib (ABT-888) is a potent PARP inhibitor, inhibiting PARP1 and PARP2 with Kᵢs of 5.2 and 2.9 nM, respectively[1].

**IC₅₀ & Target**

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>PARP-2 2.9 nM (Ki)</th>
<th>PARP-1 5.2 nM (Ki)</th>
<th>Autophagy</th>
</tr>
</thead>
</table>

**In Vitro**

Veliparib (ABT-888) is also tested against SIRT2, an enzyme that also uses NAD⁺ for catalysis, and found to be inactive (>5,000
nM). The receptor profile of Veliparib is determined in a panel of 74 receptor-binding assays at a concentration of 10 μM. Veliparib displaces control-specific binding at 50% or greater at the human H1 (61%), the human 5-HT1A (91%), and the human 5-HT7 (84%) sites only. The IC50s for these three receptors are 5.3, 1.5, and 1.2 μM, respectively[1]. c-Met knockdown cells show 4.2- (shMet-A; 95% CI=4.0-4.5) or 4.6-fold (shMet-B; 95% CI=4.4-4.8) growth inhibition when treated with 60 μM Veliparib (ABT-888). When treated with 38 μM Veliparib, c-Met knockdown cells show 2- (shMet-A; 95% CI=1.5-2.5) or 1.9-fold (shMet-B; 95% CI=1.3-2.5) growth inhibition[2]. In HaCaT cells, at 6 h post-treatment by Veliparib (ABT-888), cell viability is significantly increases under 1,000 μM sulfur mustard (SM) exposure, whereas Veliparib does not protect cell viability under 100 μM SM exposure. Moreover, the addition of Veliparib no longer shows the protective effect at 24 h post SM exposure[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo
Veliparib (ABT-888) is a potent inhibitor of PARP, has good oral bioavailability, can cross the blood-brain barrier in syngeneic and xenograft tumor models[1]. In MDA-MB-231 xenograft tumor models, combination treatment (AG014699/PF-02341066 and Veliparib (ABT-888)/Foretinib) substantially reduced tumor growth compared to either inhibitor alone[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay[2]
PARP1 enzyme activity is measured by using a commercial assay kit with the exception that cell lysates containing wild-type PARP1 or PARP Y907 mutant are used in place of the PARP1 protein included with the kit. Total lysate (500 ng) is added to each reaction. The dose course of PARP inhibitor Veliparib (ABT-888) is from 0.01 to 1,000 μM. PARP enzyme activity of wild-type and mutants is determined after incubation with the substrate is measured using a plate reader[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay[3]
Cell viability is quantified using the Cell Counting Kit-8 (CCK-8). This assay is based on Dojindo’s highly water-soluble tetrazolium salt. WST-8 is reduced by dehydrogenases in cells to give an orange, water-soluble formazan dye. The amount of the formazan dye generated by dehydrogenases in cells is directly proportional to the number of living cells. Briefly, exponentially growing HaCaT cells are seeded in 96-well plates at a density of 10,000 cells/well. 6 h or 24 h after exposure to sulfur mustard (SM) and the administration of Veliparib, the CCK-8 reagent is added[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration[2]
MDA-MB-231 (0.5×10⁶), HCC1937 (2×10⁶) or MCF-7 (5×10⁶) cells are injected into the mammary fat pads of female nude (Swiss Nu/Nu) mice of 6-8 weeks of age. A1034 (0.5×10⁶) cells are injected into the mammary fat pads of female FVB/NJ mice of 6-8 weeks of age. H1993 (0.5×10⁶) cells are injected subcutaneously into the right flank of female nude (Swiss Nu/Nu) mice of 6-8 weeks of age. When the tumor volume reaches 50 mm³, PF-02341066 (5 mg/kg) and Foretinib (5 mg/kg), AG014699 (5 mg/kg) and Veliparib (25 mg/kg), dissolved in aqueous 50 mM sodium acetate, pH 4, are administered to mice five times per week as single agents or in combination for the number of days specified in the figure legend. Tumor is measured at the indicated time points, and tumor volume is calculated by the formula: π/6×length×width². For MDA-MB-231 and A1034 xenograft mouse models, mice are imaged before and after treatment using the IVIS Imaging System to assess tumor growth. Mice are injected with 100 μL of D-luciferin (15 mg/mL in PBS). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Discov. 2017 Sep;7(9):984-998.
REFERENCES

