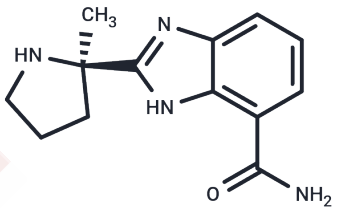
Data Sheet (Cat.No.T2591)

TargetMol

Veliparib

Chemical Properties



CAS No. : 912444-00-9

Formula: C13H16N4O

Molecular Weight: 244.29

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Veliparib (ABT-888) (ABT-888) is an orally bioavailable inhibitor of PARP (Kis: 5.2/2.9 nM for PARP1/2). It enhances apoptosis and autophagy.
Targets(IC50)	Autophagy,PARP
In vitro	Veliparib (ABT-888) is a potent inhibitor of both PARP-1 and PARP-2 with K(i)s of 5.2 and 2.9 nmol/L, respectively [1]. In the HaCaT cell model, ABT-888 can reduce SM-induced NAD(+)/ATP depletion and apoptosis/necrosis [2]. ABT-888 reduced clonogenic survival in H460 lung cancer cells and inhibited DNA repair as shown by enhanced expression of DNA strand break marker histone gamma-H2AX [3].
In vivo	PARP inhibition dramatically increased the efficacy of temozolomide at Veliparib doses as low as 3.1 mg/kg/d and a maximal efficacy achieved at 25 mg/kg/d. In the MX-1 breast xenograft model (BRCA1 deletion and BRCA2 mutation), Veliparib potentiated cisplatin, carboplatin, and cyclophosphamide, causing regression of established tumors, whereas, with comparable doses of cytotoxic agents alone, only modest tumor inhibition was exhibited [1]. Veliparib increased tumor growth delay at well-tolerated doses in murine models. For a 5-fold increase in tumor volume, tumor growth delay was 1 day for Veliparib alone, 7 days for radiation alone, and 13.5 days for combination treatment. A decrease in vitro endothelial tubule formation with Veliparib/radiation combination treatment and von Willebrand factor staining of tumor sections revealed decreased vessel formation in vivo [3].
Kinase Assay	PARP assays were conducted in a buffer containing 50 mmol/L Tris (pH 8.0), 1 mmol/L DTT, 1.5 μmol/L [3H]NAD+ (1.6 μCi/mmol), 200 nmol/L biotinylated histone H1, 200 nmol/L slDNA, and 1 nmol/L PARP-1 or 4 nmol/L PARP-2 enzyme. Reactions were terminated with 1.5 mmol/L benzamide, transferred to streptavidin Flash plates, and counted using a TopCount microplate scintillation counter [1].
Cell Research	Cell viability was 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 formazan dye generated by dehydrogenases in cells is directly proportional to the number of living cells. Briefly, exponentially growing HaCaT cells were seeded in 96-well plates at a density of 10,000 cells/well. 6 h or 24 h after exposure to SM and the administration of ABT-888, the CCK-8 reagent was added as recommended by the supplier [2].

Animal Research	For oral pharmacokinetic studies, ABT-888 was separated from plasma and brain homogenate using liquid-liquid extraction with a mixture of ethyl acetate and hexane at alkaline pH. ABT-888 and the internal standard were separated from each other and coextracted contaminants on a 50 × 3 mm Keystone Betasil Cyano 5 µm C18 column with acetonitrile: 0.1% trifluoroacetic acid mobile phase (40:60, by volume) at a flow rate of 0.3 mL/min. Analysis was done on a Sciex API3000 Biomolecular Mass Analyzer with a turbo-ionspray interface using Sciex MacQuan software. The analysis of plasma pharmacokinetics from osmotic minipump (OMP) studies was conducted using acidified methanol precipitated plasma. Samples were injected onto a Phenomenex Synergi 4µ Polar RP column and ABT-888 eluted with a mixture of acetonitrile and 0.1% acetic acid in water at a flow rate of 0.4 mL/min. Mass analysis was done with a ThermoFinnigan LCQ Duo using Xcalibur software [1].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 50 mg/mL (204.67 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (8.19 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	4.0935 mL	20.4675 mL	40.935 mL
5 mM	0.8187 mL	4.0935 mL	8.187 mL
10 mM	0.4093 mL	2.0467 mL	4.0935 mL
50 mM	0.0819 mL	0.4093 mL	0.8187 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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Mao K, Chen J, Yu H, et al. Poly (ADP-ribose) polymerase 1 inhibition prevents neurodegeneration and promotes α-synuclein degradation via transcription factor EB-dependent autophagy in mutant α-synucleinA53T model of Parkinson's disease[J]. Aging Cell. 2020: e13163.
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Epub 2020 May 31. PARP1 inhibition prevents neurodegeneration and promotes α-synuclein degradation via TFEB-dependent autophagy in mutant α-synucleinA53T model of Parkinson's disease. aging cell. 2020 Jun;19(6):e13163