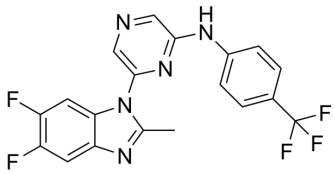
PTC-028

Cat. No.:	HY-103696
CAS No.:	1782970-28-8
Molecular Formula:	$C_{19}H_{12}F_5N_5$
Molecular Weight:	405.32
Target:	Apoptosis
Pathway:	Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (308.40 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4672 mL	12.3359 mL	24.6719 mL
5 mM	0.4934 mL	2.4672 mL	4.9344 mL
10 mM	0.2467 mL	1.2336 mL	2.4672 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: ≥ 2.08 mg/mL (5.13 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PTC-028 is an orally bioavailable inhibitor of stem cell factor BMI-1 in ovarian cancer. PTC-028 selectively inhibits cancer cells whereas normal cells remain unaffected. PTC-028 downregulates BMI-1, inducing caspase-mediated apoptosis[1].

IC_{50} & Target

BMI-1[1]

In Vitro

PTC-028 (25-500 nM; 48 hours) significantly decreases CP20, OVCAR4 and OV90 epithelial ovarian cancer cells viability. However, in normal ovarian surface epithelial cells (OSE) and fallopian tube epithelial cells (FTE) cells, up to 500 nM treatment with PTC-028 for 48 hours has minimal effect (~18-30% decrease)[1].

PTC-028 (100 nM; 2-12 hours) increases the phosphorylated BMI-1 species in a time-dependent manner. PTC-028 subsequently reduces BMI-1 in the biochemical functional readout [1].

uH2A is observed up to 12 h with PTC-028 (100 nM) in both CP20 and OV90 cells while total H2A levels remain unchanged [1].
PTC-028 (100 nM; 48 hours) decreases the expression of XIAP and RIPK1 while LC3B levels remains unchanged compared to that of the control [1].
Significant cleavage of Caspase 7, Caspase 9 and PARP is observed in PTC-028 (100 nM; 48 hours)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	OVCAR4, OV90 and CP20 cells
Concentration:	0, 25, 50, 100, 200, 500 nM
Incubation Time:	48 hours
Result:	OVCAR4, OV90 and CP20 cells demonstrated significant dose dependent decrease in cell viability with an IC_{50} of ~100 nM and ~95% decrease at 500 nM.

Western Blot Analysis[1]

Cell Line:	OV90 and CP20 cells
Concentration:	100 nM
Incubation Time:	2, 4, 6, 12 hours
Result:	A time-dependent increase in the phosphorylated BMI-1 species and subsequent reduction in the biochemical functional readout. uH2A was observed up to 12 h while total H2A levels remained unchanged.

In Vivo

PTC-028 (15 mg/kg; administered orally twice weekly) causes ~94% (0.169 g) reduction in tumor weight compared to the control (average tumor weight, ~3g) [1].
No obvious toxicity is noted in the animals during therapy experiments as assessed by mean body weight[1].
PTC-028 (10 mg/kg or 20mg/kg; single oral doses) is administrated to the CD-1 mice. The C_{max} is reached at both dose levels 1h post dose after which plasma concentrations slowly reduce[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female athymic nude mice with implanted OV90 cells[1]
Dosage:	15 mg/kg
Administration:	Orally administered; twice weekly
Result:	Caused ~94% (0.169 g) reduction in tumor weight.

Animal Model:	Female CD-1 mice[1]
Dosage:	10 mg/kg or 20mg/kg
Administration:	Oral administered; single dose
Result:	Total plasma $AUC_{0\text{-}24h}$ were 10.9 and 26.1 μg•h/mL at doses of 10 and 20 mg/kg. The C_{max} for PTC-028 at 10 and 20 mg/kg was 0.79 and 1.49 ug/mL, respectively.

REFERENCES

[1]. Dey A, et al. Evaluating the Mechanism and Therapeutic Potential of PTC-028, a Novel Inhibitor of BMI-1 Function in Ovarian Cancer. Mol Cancer Ther. 2018 Jan;17(1):39-49.

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