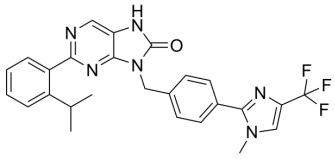
I-138

Cat. No.:	HY-153365
CAS No.:	2098211-50-6
Molecular Formula:	$C_{26}H_{23}F_3N_6O$
Molecular Weight:	492.5
Target:	Deubiquitinase
Pathway:	Cell Cycle/DNA Damage
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 : 100 mg/mL (203.05 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0305 mL	10.1523 mL	20.3046 mL
5 mM	0.4061 mL	2.0305 mL	4.0609 mL
10 mM	0.2030 mL	1.0152 mL	2.0305 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: 2.5 mg/mL (5.08 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.08 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

I-138 is an orally active, reversible inhibitor of USP1-UAF1 (IC50: 4.1 nM; Ki: 5.4 nM), structurally related to ML323 (HY-17543). I-138 induces monoubiquitination of FANCD2 and PCNA in cells and eliminates USP1 autocleavage in cells[1].

In Vitro

I-138 (0.5 μM; 4 h) eliminates USP1 self-lysis in HAP-1 USP1 WT and knockout cells[1].
I-138 (0.5 μM; 4 h) induces the monoubiquitination of FANCD2 and PCNA in MDA-MB-436 cells[1].
(0.01-10 μM; 10 days) dose-dependently inhibits MDA-MB-436 cells viability and don't affect HCC1954 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

I-138 (50 mg/kg/day; po, for 41 days) results USP1 inhibition and modest antitumor activity in mice bearing MDA-MB-436 tumors. However, the combination of I-138 and Niraparib (HY-10619), a PARP inhibitor, benefit the BRCA1/2 mutant tumors

inhibition in vivo[1].

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

REFERENCES

[1]. Simoneau A, et al. Ubiquitinated PCNA Drives USP1 Synthetic Lethality in Cancer. Mol Cancer Ther. 2023 Feb 1;22(2):215-226.

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