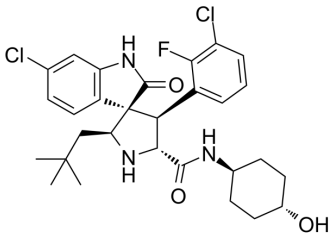
SAR405838

Cat. No.:	HY-18986
CAS No.:	1303607-60-4
Molecular Formula:	$C_{29}H_{34}Cl_2FN_3O_3$
Molecular Weight:	562.5
Target:	MDM-2/p53; E1/E2/E3 Enzyme
Pathway:	Apoptosis; Metabolic Enzyme/Protease
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 (177.78 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7778 mL	8.8889 mL	17.7778 mL
	5 mM	0.3556 mL	1.7778 mL	3.5556 mL
	10 mM	0.1778 mL	0.8889 mL	1.7778 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 (4.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.44 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SAR405838 is a highly potent and selective MDM2 inhibitor, binds to MDM2 with Ki= 0.88 nM and has high specificity over other proteins.IC50 value: 0.88 nM (Ki) [1]Target: MDM2in vitro: SAR405838 potently inhibits cell growth in cancer cell lines, including SJSA-1 (IC50, 0.092 μM), RS4;11 (IC50, 0.089 μM), LNCaP (IC50, 0.27 μM), and HCT-116 (IC50, 0.20 μM) cells, and displays high selectivity over cancer cell lines with mutated or deleted p53, including SAOS-2 (IC50, >10 μM), PC-3 (IC50, >10 μM), SW620 (IC50, >10 μM), and HCT-116 (p53-/-) (IC50, >20 μM) cells.[1] SAR405838 effectively induces apoptosis in the RS4;11 cell line. SAR405838 potently inhibits cell growth and induces dose-dependent apoptosis in the ABTR1 and ABTR2 sublines, albeit with modestly reduced potency compared with that in the control RS4;11 cell line.[2]in vivo: At well-

tolerated dose schedules, SAR405838 achieves either durable tumor regression or complete tumor growth inhibition in mouse xenograft models of SJSA-1 osteosarcoma, RS4;11 acute leukemia, LNCaP prostate cancer and HCT-116 colon cancer. Remarkably, a single oral dose of SAR405838 is sufficient to achieve complete tumor regression in the SJSA-1 model. In the SJSA-1 osteosarcoma, acute lymphoblastic leukemia RS4;11, LNCaP prostate cancer, and HCT-116 colon cancer xenograft model, MI-773 (p.o.) effectively inhibits tumor growth in a dose-dependent manner (10 mg/kg, 30 mg/kg, 50 mg/kg, 100 mg/kg, and 200 mg/kg,). [1]

REFERENCES

[1]. Wang S, et al. SAR405838: an optimized inhibitor of MDM2-p53 interaction that induces complete and durable tumor regression. Cancer Res. 2014 Oct 15;74(20):5855-5865.

[2]. Hoffman-Luca CG, et al. Elucidation of Acquired Resistance to Bcl-2 and MDM2 Inhibitors in Acute Leukemia In Vitro and In Vivo. Clin Cancer Res. 2015 Jun 1;21(11):2558-2568.

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