# SAR405838

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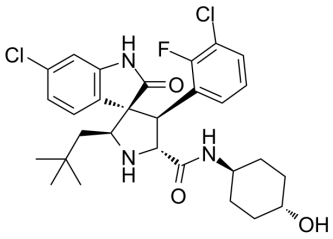
|---|---|
| **Cat. No.:** | HY-18986 |
| **CAS No.:** | 1303607-60-4 |
| **Molecular Formula:** | $C_{29}H_{34}Cl_2FN_3O_3$ |
| **Molecular Weight:** | 562.5 |
| **Target:** | MDM-2/p53; E1/E2/E3 Enzyme |
| **Pathway:** | Apoptosis; Metabolic Enzyme/Protease |
| **Storage:** | Powder -20°C 3 years<br>4°C 2 years<br>In solvent -80°C 6 months<br>-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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