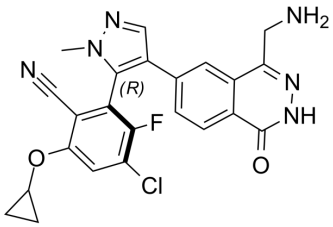
MRTX-1719

Cat. No.:	HY-139611
CAS No.:	2630904-45-7
Molecular Formula:	$C_{23}H_{18}ClFN_6O_2$
Molecular Weight:	464.88
Target:	Histone Methyltransferase
Pathway:	Epigenetics
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 (215.11 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1511 mL	10.7555 mL	21.5109 mL
	5 mM	0.4302 mL	2.1511 mL	4.3022 mL
	10 mM	0.2151 mL	1.0755 mL	2.1511 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 mg/mL (4.30 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2 mg/mL (4.30 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2 mg/mL (4.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MRTX-1719 is a potent, orally active, selective PRMT5•MTA complex inhibitor, with IC_{50} of 3.6 and 20.5 nM for PRMT5•MTA and PRMT5. MRTX-1719 binds to the PRMT5•MTA complex, with KD value of 0.14 pM. MRTX-1719 shows antineoplastic activity in vitro and in vivo, and can be used for cancer study[1][2].

IC_{50} & Target

PRMT5

In Vitro

MRTX-1719 (10 day) inhibits the PRMT5 activity and in MTAP-deleted HCT116 cells not wild type cells, with the IC_{50} of 8 nM[1]

.MRTX1719 (10 day) inhibits the cell viability of MTAP del HCT116 cells with an IC_{50} value of 12 nM and parental HCT116 cells with an IC_{50} value of 890 nM[1].

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

In Vivo

MRTX1719 (12.5-100 mg/kg/d for p.o., 21 day) reduces the tumor growth in Lu-99 orthotopic xenograft tumor models[2].

Pharmacokinetic Analysis [2]

Model	Route	Dose (mg/kg)	Cl_{total} (mL/min/kg)	V_{dss} (L/kg)	$t_{1/2}$ (h)
CD-1 mouse.	i.v.	3	83	6.3	1.5
Beagle dog	i.v.	2	14	3.4	4.8
Cynomolgus monkey	i.v.	2	15	2.3	6.1

Model	Route	Dose (mg/kg)	C_{max} (ug/mL)	AUC_{inf} (h*ug/mL)	F (%)
CD-1 mouse.	p.o.	30	1.16	4.85	80
Beagle dog	p.o.	10	1.40	7.47	59
Cynomolgus monkey	p.o.	10	/	/	41

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

Animal Model:	Lu-99 (an MTAP/CDKN2A-deleted human lung cancer cell line) xenograft tumor models[2]
Dosage:	12.5, 25, 50, and 100 mg/kg/d, 21 day
Administration:	Oral gavage
Result:	Reduced the tumor volume with 86% tumor growth inhibition (TGI) at 50 mg/kg and 88% TGI at 100 mg/kg.

REFERENCES

[1]. 1. Lars D Engstrom, et al. MRTX1719 is an MTA-cooperative PRMT5 inhibitor that exhibits synthetic lethality in preclinical models and patients with MTAP deleted cancer. Cancer Discov. 2023 Aug 8;CD-23-0669.

[2]. Christopher R Smith, et al. Fragment-Based Discovery of MRTX1719, a Synthetic Lethal Inhibitor of the PRMT5•MTA Complex for the Treatment of MTAP-Deleted Cancers. J Med Chem. 2022 Feb 10;65(3):1749-1766.

[3]. Targeting the genetic and immunological drivers of cancer.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA