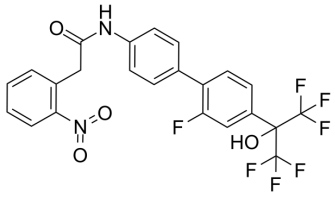
XY018

Cat. No.:	HY-120210
CAS No.:	1873358-87-2
Molecular Formula:	$C_{23}H_{15}F_7N_2O_4$
Molecular Weight:	516.37
Target:	ROR
Pathway:	Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor
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 : 100 mg/mL (193.66 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9366 mL	9.6830 mL	19.3660 mL
5 mM	0.3873 mL	1.9366 mL	3.8732 mL
10 mM	0.1937 mL	0.9683 mL	1.9366 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

XY018 is a potent ROR-γ-selective antagonist. XY018 inhibits ROR-γ constitutive activity in 293T cells with high potency (EC_{50}, 190 nM). XY018 binds to the ROR-γ hydrophobic ligand binding domain (LBD)[1].

IC_{50} & Target

ROR-γ	ROR-α
0.19 μM (IC_{50}, in 293 T cells)	7.57 μM (IC_{50}, in 293 T cells)

In Vitro

XY018 (0.07-10 μM; 4 days) inhibit CRPC tumors C4-2B cells growth and survival[1].
XY018 inhibits Gal4-RORγ-LBD and Gal4-RORα-LBD with IC_{50}s of 0.19±0.02 and 7.57 μM in 293 T cells, respectively[2].
XY018 shows anti-proliferation effects against the prostate cancer cell lines LNCaP, 22Rv1, C4-2B, DU145, and PC-3 with IC_{50}s

of 5.14±0.36, 9.00±0.33, 9.20, 28.43±0.89, and 11.14±1.78 μM, respectively[2].

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

Cell Viability Assay[1]

Cell Line:	CRPC tumors C4-2B
Concentration:	0.07, 0.15, 0.31, 0.62, 1.25, 2.5, 5, and 10 μM
Incubation Time:	4 days
Result:	Inhibited growth and survival.

In Vivo

XY018 (5 mg/kg; intraperitoneally i.p.; five times per week for 23 days) inhibit CRPC tumor growth in mice[1] .

XY018 (10 mg/kg orally or 2 mg/kg intravenously) exhibits reasonable pharmacokinetics profiles in SD rats[2].

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

Animal Model:	Four-week-old male SCID C.B17 mice (for C4-2B and VCaP) or BALB/c nu/nu athymic mice (for 22Rv1 and PC-3)[1]
Dosage:	5 mg/kg
Administration:	Treated intraperitoneally (i.p.); five times per week for 23 days
Result:	Tumor growth inhibition.

Animal Model:	Sprague Dawley rats[2]
Dosage:	10 mg/kg (po; 1 mg/mL); 2 mg/kg (iv;0.4 mg/mL) (Pharmacokinetic Analysis)
Administration:	Orally administrated (10 mg/kg) and intravenously administrated (2 mg/kg); single dose
Result:	High plasma exposure $AUC_{(0-\infty)}$ value of 6444 (μg/L·h), half-life ($T_{1/2}$=7.67±2.36 h) and maximum plasma concentration (C_{max}) value of 839 (μg/L) after a 2 mg/kg iv administration. Demonstrated a relatively low oral bioavailability of 19% after an oral administration.

REFERENCES

[1]. Junjian Wang, et al. ROR-γ Drives Androgen Receptor Expression and Represents a Therapeutic Target in Castration-Resistant Prostate Cancer. Nat Med. 2016 May;22(5):488-96.

[2]. Yan Zhang, et al. Discovery and Characterization of XY101, a Potent, Selective, and Orally Bioavailable RORγ Inverse Agonist for Treatment of Castration-Resistant Prostate Cancer. J Med Chem. 2019 May 9;62(9):4716-4730.

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