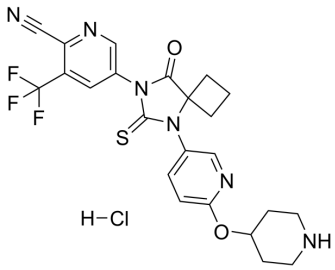
JNJ-63576253

Cat. No.:	HY-115282A
CAS No.:	2110428-64-1
Molecular Formula:	$C_{23}H_{22}ClF_3N_6O_2S$
Molecular Weight:	538.97
Target:	Androgen Receptor
Pathway:	Vitamin D Related/Nuclear Receptor
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (463.85 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8554 mL	9.2770 mL	18.5539 mL
	5 mM	0.3711 mL	1.8554 mL	3.7108 mL
	10 mM	0.1855 mL	0.9277 mL	1.8554 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: ≥ 2.08 mg/mL (3.86 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.86 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.86 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JNJ-63576253 (TRC-253) is a potent and orally active full antagonist of androgen receptor (AR), with IC_{50}s of 37 and 54 nM for F877L mutant AR and wild-type AR in LNCaP cells. JNJ-63576253 can be used for the research of castration-resistant prostate cancer (CRPC)[1].

IC_{50} & Target

IC50: 37 nM (F877L mutant AR in LNCaP cells); 54 nM (wild-type AR in LNCaP cells)[1]

In Vitro

JNJ-63576253 (0.0003-100 μM; 5 d) inhibits the growth of VCaP cells, with an IC_{50} of 265 nM[1].
JNJ-63576253 is stable in human liver microsomes, with an T1/2 of >180 min[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

JNJ-63576253 (30 mg/kg; p.o. once daily for 72 days) significantly inhibits the growth of prostate LNCaP SRα F877L tumor in mice[1].

JNJ-63576253 (30 mg/kg; p.o. once daily for 10 days) inhibits the five androgen sensitive organs (ASOs) under stimulation by testosterone propionate (TP) in mice[1].

JNJ-63576253 (10 mg/kg; p.o.) exhibits moderate oral bioavailability (45%), C_{max} (0.66 μM) and AUC_{last} (4.9 μg h/mL) in mice[1].

JNJ-63576253 (2 mg/kg; i.v.) exhibits reasonable half-life (5.99 h), CL (15.0 mL/min/kg) and Vdss (6.11 L/kg) in mice[1].

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

Animal Model:	Castrated SHO mice with prostate LNCaP SRα F877L tumor[1]
Dosage:	30 mg/kg
Administration:	P.o. once daily for 72 days
Result:	Inhibited the tumor growth by 87%.

Animal Model:	CD-1 male mice[1]
Dosage:	2 mg/kg for i.v.; 10 mg/kg for p.o. (Pharmacokinetic Analysis)
Administration:	Intravenous administration and oral administration
Result:	I.v.: T1/2=5.99 h; CL=15.0 mL/min/kg; Vdss=6.11 L/kg. P.o.: F=45%; C_{max}=0.66 μM; AUC_{last}=4.9 μg•h/mL.

CUSTOMER VALIDATION

- Eur J Med Chem. 2023 Jan 14;249:115110.

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REFERENCES

[1]. Zhang Z, et, al. Discovery of JNJ-63576253: A Clinical Stage Androgen Receptor Antagonist for F877L Mutant and Wild-Type Castration-Resistant Prostate Cancer (mCRPC). J Med Chem. 2021 Jan 28;64(2):909-924.

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