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产品名称：JNJ-63576253
CAS 号：2110426-27-0
产品货号：S89192

生物活性：

Description

JNJ-63576253 (TRC-253) free base 是一种有效和具有口服活性的雄激素受体 (androgen receptor) 的完全拮抗剂，在 LNCaP 细胞中对 F877L 突变型 AR 和野生型 AR 的 IC50 值分别为 37 和 54 nM。JNJ-63576253 free base 可用于去势抵抗性前列腺癌 (CRPC) 的研究。

IC50 & Target

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

Cellular Effect

Cell Line	Type	Value	Description
VCaP	IC_{50}	265 nM	Antiproliferative activity against human VCaP cells expressing wild-type androgen receptor assessed as reduction in cell viability incubated for 5 days in presence of R1881 by CellTiter-glo assay
VCaP	IC_{50}	290 nM	Antiproliferative activity against human VCaP cells

In Vitro

JNJ-63576253 (0.0003-100 μM; 5 d) inhibits the growth of VCaP cells, with an IC50 of 265 nM[1].

JNJ-63576253 is stable in human liver microsomes, with an T1/2 of >180 min[1].

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%), Cmax (0.66 μM) and AUClast (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].

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.: $T_{1/2}$=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.

参考文献

[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.