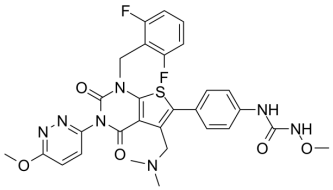
Relugolix

Cat. No.:	HY-16474
CAS No.:	737789-87-6
Molecular Formula:	$C_{29}H_{27}F_2N_7O_5S$
Molecular Weight:	623.63
Target:	GnRH Receptor
Pathway:	GPCR/G Protein
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 (160.35 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6035 mL	8.0176 mL	16.0351 mL
	5 mM	0.3207 mL	1.6035 mL	3.2070 mL
	10 mM	0.1604 mL	0.8018 mL	1.6035 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: ≥ 0.83 mg/mL (1.33 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.83 mg/mL (1.33 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.83 mg/mL (1.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Relugolix (TAK-385) is a potent, orally active, nonpeptidic gonadotropin-releasing hormone (GnRH) antagonist. Relugolix possesses high affinity and potent antagonistic activity for human receptor (binding IC_{50}=0.33 nM) and monkey receptor (IC_{50}=0.32 nM) compared with TAK-013 (HY-100209)[1]. Relugolix is used for the study of sex-hormone-dependent diseases, such as including endometriosis, uterine fibroids and prostate cancer et al[2].

IC_{50} & Target

IC50: 0.33 nM (human GnRH)
IC50: 0.32 nM (monkey GnRH)[2]

In Vitro

Relugolix exhibits strong binding affinity (IC_{50}=0.32 nM) for the monkey receptor comparable to that for the human receptor (IC_{50}=0.33 nM) while displaying a 30000-fold decrease for the rat receptor (IC_{50}=9800 nM). The antagonistic in vitro activity of TAK-385 with respect to the human receptor (IC_{90}=18 nM) exceeded that for the monkey receptor (IC_{90}=1700 nM) by 95-fold in the presence of 40% serum[1].

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

In Vivo

Relugolix (oral administration; 1-3 mg/kg; single dose for pharmacokinetic study) exhibits a good pharmacokinetic profile and obvious suppressive effects of circulating LH levels in monkeys at a dose of 1 mg/kg. The pharmacokinetic profile exhibits with 16.0 ng/mL, 2.7 h, and 90.1 ng for C_{max}, T_{max}, and AUC_o, respectively in male cynomolgus monkeys[1].

Relugolix (oral administration; 3, 10 or 30 mg/kg; twice daily; 4 weeks) significantly decreases the testis weight, and reduces the ventral prostate weight at 3 mg/kg and decreases it to castrate levels at 10 mg/kg in male hGNRHR-knock-in mice[2].

Relugolix (oral administration; 30, 100 or 200 mg/kg; twice daily; 4 weeks) induces constant diestrous phases in all mice within the first week at 100 mg/kg, and significantly decreases the weights of ovaries and uteri at this dose after 4 weeks in female hGNRHR-knock-in mice[2].

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

Animal Model:	Male hGNRHR-knock-in mice[2]
Dosage:	3, 10 or 30 mg/kg
Administration:	Oral administration; 3, 10 or 30 mg/kg; twice daily; 4 weeks
Result:	Decreased testicular function.

Animal Model:	Female hGNRHR-knock-in mice[2]
Dosage:	30, 100 or 200 mg/kg
Administration:	Oral administration; 30, 100 or 200 mg/kg; twice daily; 4 weeks
Result:	Suppressed the hypothalamic–pituitary–gonadal axis to gonadectomized levels. Downregulated GnRH receptor mRNA levels in the pituitary.

REFERENCES

[1]. Kazuhiro Miwa, et al. Discovery of 1-{4-[1-(2,6-Difluorobenzyl)-5-[(dimethylamino)methyl]-3-(6-methoxypyridazin-3-yl)-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidin-6-yl]phenyl}-3-methoxyurea (TAK-385) as a Potent, Orally Active, Non-Peptide Antagonis

[2]. Daisuke Nakata, et al. Suppression of the hypothalamic-pituitary-gonadal axis by TAK-385 (relugolix), a novel, investigational, orally active, small molecule gonadotropin-releasing hormone (GnRH) antagonist: studies in human GnRH receptor knock-in mice. E

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