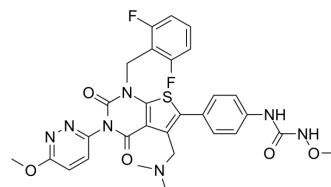


Relugolix

Cat. No.:	HY-16474		
CAS No.:	737789-87-6		
Molecular Formula:	C ₂₉ H ₂₇ F ₂ N ₇ O ₅ S		
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	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (160.35 mM; Need ultrasonic)

Concentration	Solvent	Mass	1 mg			5 mg			10 mg		
			Concentration			Concentration			Concentration		
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

- 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
- 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
- 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 IC₅₀=0.33 nM) and monkey receptor (IC₅₀=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].

IC₅₀ & Target

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

<p>In Vitro</p>	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>																
<p>In Vivo</p>	<p>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_0, respectively in male cynomolgus monkeys^[1].</p> <p>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 hGHRHR-knock-in mice^[2].</p> <p>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 hGHRHR-knock-in mice^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1" data-bbox="345 659 1515 898"> <tr> <td>Animal Model:</td> <td>Male hGHRHR-knock-in mice^[2]</td> </tr> <tr> <td>Dosage:</td> <td>3, 10 or 30 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>Oral administration; 3, 10 or 30 mg/kg; twice daily; 4 weeks</td> </tr> <tr> <td>Result:</td> <td>Decreased testicular function.</td> </tr> </table> <table border="1" data-bbox="345 936 1515 1205"> <tr> <td>Animal Model:</td> <td>Female hGHRHR-knock-in mice^[2]</td> </tr> <tr> <td>Dosage:</td> <td>30, 100 or 200 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>Oral administration; 30, 100 or 200 mg/kg; twice daily; 4 weeks</td> </tr> <tr> <td>Result:</td> <td>Suppressed the hypothalamic-pituitary-gonadal axis to gonadectomized levels. Downregulated GnRH receptor mRNA levels in the pituitary.</td> </tr> </table>	Animal Model:	Male hGHRHR-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 hGHRHR-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.
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REFERENCES

- [1]. Kazuhiro Miwa, et al. Discovery of 1-[4-[1-(2,6-Difluorobenzyl)-5-[(dimethylamino)methyl]-3-(6-methoxy-pyridazin-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 Antagonist of the Human Gonadotropin-Releasing Hormone Receptor. doi/10.1021/jm200216q
- [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. Eur J Pharmacol. 2014 Jan 15;723:167-74.

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