NBI-42902

Cat. No.: HY-13699

CAS No.: 352290-60-9

Molecular Formula: $C_{27}H_{24}F_3N_3O_3$

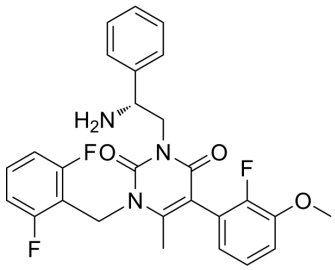
Molecular Weight: 495.49

Target: GnRH Receptor; PERK

Pathway: GPCR/G Protein; Cell Cycle/DNA Damage

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 (201.82 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0182 mL	10.0910 mL	20.1820 mL
	5 mM	0.4036 mL	2.0182 mL	4.0364 mL
	10 mM	0.2018 mL	1.0091 mL	2.0182 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: 2.5 mg/mL (5.05 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.05 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.05 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

NBI-42902 is an orally active, potent functional and competitive antagonist of GnRH receptor with an IC_{50} value of 0.79 nM, a K_i value of 0.56 nM, respectively. NBI-42902 inhibits GnRH-stimulated inositol phosphate (IP) accumulation, Ca^{2+} flux, and ERK1/2 activation. NBI-42902 inhibits serum luteinizing hormone (LH) in castrated male macaques. NBI-42902 can be used for research on sex-hormone-related diseases[1].

In Vitro

NBI-42902 (0-1000 nM) is quite sensitive to the relatively conservative sequence changes between species, with IC_{50} values of 0.79 nM (human), 10 nM (macaque), 400 nM (dog), 200 nM (rabbit) for the GnRH receptors[1].

NBI-42902 (1 nM-1 μM, 1 min) inhibits GnRH (4 nM)-stimulated Ca^{2+} flux in RBL cells with a mean IC_{50} value of 3.6 nM[1].
NBI-42902 (1 nM-1 μM, 1 min) inhibits GnRH (4 nM)-induced IP accumulation competitively in RBL cells[1].
NBI-42902 (1 nM-1 μM, 5 min) blocks GnRH-stimulated ERK1/2 phosphorylation completely in CHO-GnRHR cells with an IC_{50} value of 5.22 nM[1].

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

Western Blot Analysis[1]

Cell Line:	CHO-GnRHR
Concentration:	1 nM-1 μM
Incubation Time:	5 min
Result:	Blocked GnRH (1 nM)-stimulated ERK1/2 phosphorylation completely in a dose-dependent manner, with an IC_{50} value of 5.22 nM.

In Vivo

NBI-42902 (10-100 mg/kg, p.o. or i.v.) inhibits serum LH levels significantly in castrated macaques[1].

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

Animal Model:	Castrated macaques[1]
Dosage:	10, 40, 100 mg/kg
Administration:	Oral administration (p.o.)
Result:	Inhibited serum LH with dose dependent. Inhibited serum LH achieved maximum suppression, that was 62-68% of pretreatment baseline, at 4-8 h after administration. Exhibited no suppression of LH levels after 24 h treated with 10 or 40 mg/kg, but remained suppression at 100 mg/kg.

Animal Model:	Castrated macaques[1]
Dosage:	10 mg/kg
Administration:	Intravenous injection (i.v.)
Result:	Inhibited serum LH achieved maximum suppression was 62-68% of pretreatment baseline between 4-8 h after administration, but exhibited no suppression after 24 h.

REFERENCES

[1]. Struthers RS, et al. Pharmacological characterization of a novel nonpeptide antagonist of the human gonadotropin-releasing hormone receptor, NBI-42902. Endocrinology. 2007 Feb;148(2):857-67.

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