Orforglipron

Cat. No.: HY-112185

CAS No.: 2212020-52-3

Molecular Formula: $C_{48}H_{48}F_2N_{10}O_5$

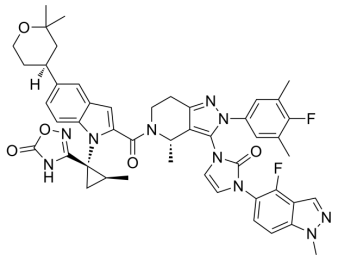
Molecular Weight: 882.96

Target: GCGR

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 (113.26 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1326 mL	5.6628 mL	11.3255 mL
	5 mM	0.2265 mL	1.1326 mL	2.2651 mL
	10 mM	0.1133 mL	0.5663 mL	1.1326 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 mg/mL (2.27 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2 mg/mL (2.27 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Orforglipron (LY3502970) (Compound 67) is an orally active agonist for Glucagon-like peptide-1 receptor (GLP-1R), which exhibits potency in ameliorates the type 2 diabete[1].

IC_{50} & Target

GLP-1 receptor[1]

In Vitro

Orforglipron is an incretin secreted from L cells of the small intestine when nutrients pass through the digestive tract, and glucose is transmitted via the GLP-1 receptor. Orforglipron exhibits various actions such as dependent gastric emptying delay, and feeding suppression[1].

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

In Vivo

Orforglipron (0.94-4.8 nM in plasma concentration, i.v., or 0.05-0.1 mg/mL, i.g. for 5 days) suppresses food intake in a dose-dependent manner, promotes insulin secretion and decreases blood glucose in cynomolgus monkey model[1].
Orforglipron (0.05-1.35 mg/kg, i.g.) reaches C_{max} 2 hours after administration at all doses, exhibits proportional ratio of increase in plasma drug exposure to dose increase, indicates a dose-dependent absorption in the gastrointestinal tract[1].

Pharmacokinetic Analysis of Orforglipron in cynomolgus monkey [1]

route	Dose (mg/kg)	T_{max} (h)	C_{max} (ng/mL)	AUC_{0-24h} (ng·h/mL)
i.g.	0.05	2.0	4.78	23.7
i.g.	0.15	2.0	20.7	135
i.g.	0.45	2.0	32.0	208
i.g.	1.35	2.0	148	1040

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

Animal Model:	cynomolgus monkey model[1]
Dosage:	0.9-4.8 nM; 0.05-0.1 mg/mL
Administration:	continuous i.v. administration for 30 minutes until a plasma concentration of 0.9-4.8 nM at steady state; i.g. for 5 days with dose of 0.05-0.1 mg/mL
Result:	Increased insulin secretion and decreased plasma-glucose.Suppressed food intake in a dose-dependent manner.

REFERENCES

[1]. Pyrazolopyridine derivative having glp-1 receptor agonist effect. WO2018056453A1

[2]. Kawai T, Sun B, Yoshino H, et al. Structural basis for GLP-1 receptor activation by LY3502970, an orally active nonpeptide agonist. Proc Natl Acad Sci U S A. 2020;117(47):29959-29967.

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