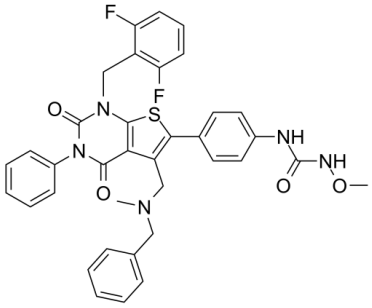
Data Sheet

Product Name:	Sufugolix
Cat. No.:	CS-6434
CAS No.:	308831-61-0
Molecular Formula:	C36H31F2N5O4S
Molecular Weight:	667.72
Target:	Others
Pathway:	Others
Solubility:	DMSO : 1.25 mg/mL (1.87 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Sufugolix (TAK-013) is a highly potent and orally available luteinizing hormone-releasing hormone (**LHRH**) receptor antagonist with an **IC_{50}** of 0.1 nM. IC50 & Target: IC50: 0.1 nM (human LHRH), 0.6 nM (monkey LHRH)[1] **In Vitro:** Sufugolix exhibits more than 3- and 2000-fold selectivity for the human receptor over the monkey and rat receptors, respectively. Sufugolix effectively antagonizes LHRH function on CHO cells expressing the human (IC_{50}=0.1 nM) and monkey (IC_{50}=0.6 nM) receptors. During the conformational analysis of sufugolix, using high-temperature molecular dynamics calculation, it is observed that the cis conformer of the methoxyurea is more populated than the trans conformer [1]. **In Vivo:** Oral administration of sufugolix causes almost complete suppression of the plasma LH levels in castrated male cynomolgus monkeys at a 30 mg/kg dose with sufficient duration of action (more than 24 h). The maximum plasma concentrations of sufugolix are 0.34 μM (reached 6 h after administration) and 0.18 μM (reached 4 h after administration) at 30 and 10 mg/kg doses, respectively[1].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]The receptor-expressing CHO cells are seeded into 24-well plates at a density of 4×10^4 cells/well and cultured for 1 day. The cells are then incubated with [5,6,8,9,11,12,14,15-^{3}H]arachidonic acid (11 kBq/well) for 1 day and ished with DMEM supplemented with 20 mM HEPES and 0.2% BSA. The cells are then preincubated with the compounds (Sufugolix) at 37 °C for 60 min and the reaction is started by addition of LHRH (1 nM). After incubation at37 °C for 40 min, radioactivity in the medium is measured with a liquid scintillation counter[1]. **Animal Administration:** [1]Monkeys: Sufugolix (10 or 30 mg/kg, 3 mL/kg, n=3 for each group) is suspended in 0.5% methylcellulose containing 1.2% citric acid, or 0.5% methylcellulose containing 1.2% citric acid alone (3 mL/kg, n=3), are administered orally. Blood samples (heparin-plasma) are collected from a femoral vein 24 h before administration and 0, 2, 4, 8, 24, and 48 h after administration. LH concentrations in the plasma are measured by bioassays using mouse testicular cells[1].

References:

[1]. Sasaki S, et al. Discovery of a thieno[2,3-d]pyrimidine-2,4-dione bearing a p-methoxyureidophenyl moiety at the 6-position: a highly potent and orally bioavailable non-peptide antagonist for the human luteinizing hormone-releasing hormone receptor. J Med Chem. 2003 Jan 2;46(1):113-24.

CAIndexNames:

Urea, N-[4-[1-[(2,6-difluorophenyl)methyl]-1,2,3,4-tetrahydro-5-[[methyl(phenylmethyl)amino]methyl]-2,4-dioxo-3-phenylthieno[2,3-d]pyrimidin-6-yl]phenyl]-N'-methoxy-

SMILES:

O=C(NOC)NC1=CC=C(C(S2)=C(CN(C)CC3=CC=CC=C3)C(C(N4C5=CC=CC=C5)=O)=C2N(CC6=C(F)C=CC=C6F)C4=O)C=C1

Caution: Product has not been fully validated for medical applications. For research use only.

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