Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

Nirogacestat

Catalog No: tcsc1689

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
1290543-63-3

Formula:
$C_{27}H_{41}F_2N_5O$

Pathway:
Stem Cell/Wnt;Neuronal Signaling

Target:
γ-secretase;γ-secretase

Purity / Grade:
>98%

Solubility:
H2O :

Alternative Names:
PF-3084014;PF-03084014

Observed Molecular Weight:
489.64

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Product Description

Nirogacestat (PF-3084014) is a reversible, noncompetitive, and selective **γ-secretase** inhibitor with **IC_{50}** of 6.2 nM.

IC50 & Target: IC50: 6.2 nM (γ-secretase)[1]

In Vitro: The IC_{50} of Nirogacestat (PF-03084014) for γ-secretase enzyme inhibition in cell-free assay for Aβ production using detergent solubilized membranes derived from HeLa cells is determined to be 6.2 nM. When tested for inhibition of Notch receptor cleavage in cellular assays using HPB-ALL cells that harbor mutations in both the heterodimerization and PEST domains in Notch1, the cell IC_{50} is determined to be 13.3 nM. Nirogacestat (PF-03084014) causes a significant increase in caspase-3 activities in HPB-ALL and TALL-1 cells as well as an induction of cleaved PARP and cleaved caspase-3 after a 7-day treatment[1].

In Vivo: Nirogacestat (PF-03084014) shows robust antitumor activity in this model on 14-day twice daily dosing. Tumor growth inhibition is dose dependent, with maximal tumor growth inhibition of ~92% obtained at high dose levels (150 mg/kg). In tumor growth inhibition studies where mice receive repetitive twice daily dosing for more than a week, Nirogacestat (PF-03084014) is well tolerated at dose levels below 100 mg/kg as no significant weight loss, morbidity, or mortality is observed. When the dose is increased to 150 mg/kg, however, mice have diarrhea and show weight loss (10-15%) approximately 10 days after compound administration. The body weight of treated animals usually returns to normal if dosing holidays are given, suggesting that the toxicity of Nirogacestat (PF-03084014) is reversible[1]. In the 7-day repeat dose toxicokinetic (TK) and first 1-month combination repeat dose studies, treatment with Dexamethasone alone and Dexamethasone with Nirogacestat (PF-03084014) cause moderate to marked body weight loss (-10% to -27%) after 7 days treatment. In the second 1-month combination repeat dose study, a similar magnitude of body weight loss (-10% to 22%) occurs with repeat dosing on the first week or third week of treatment with 100 mg/kg Nirogacestat (PF-03084014) and 1 mg/kg Dexamethasone. When Dexamethasone is not coadministered with Nirogacestat (PF-03084014) on the second week of study, increases (4%) in body weight are noted, suggesting that the body weight loss is reversible [2].