

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

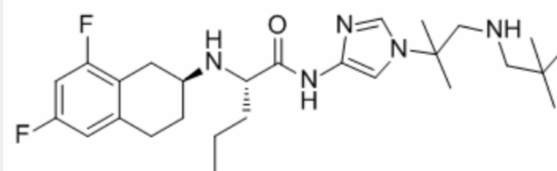
Product Description

Nirogacestat (PF-3084014) is a reversible, noncompetitive, and selective **γ -secretase** inhibitor with **IC₅₀** of 6.2 nM.

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

In Vitro: The IC₅₀ of Nirogacestat (PF-03084014) for γ -secretase enzyme inhibition in cell-free assay for A β 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 IC₅₀ 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].



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!