Product Datasheet

Nirogacestat dihydrobromide

Catalog No. **BP-01861A** · CAS **1962925-29-6** · Form **salt · hydrobromide** · Physical state **solid** · Color **White to yellow** · Version **1.0** · Revision **2026-09-02**

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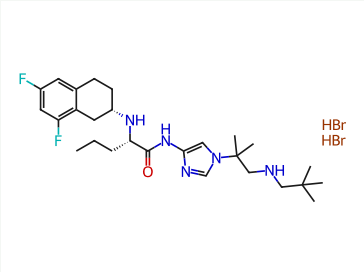
Target	Research area
γ-secretase; Apoptosis	**Cancer**

Molecular formula	$C_{27}H_{43}Br_2F_2N_5O$
Molecular weight	**651.4680**

STRUCTURE



DESCRIPTION

Nirogacestat dihydrobromide (PF-3084014 dihydrobromide) is a reversible, orally bioavailable, noncompetitive, and selective γ-secretase inhibitor with an IC50 of 6.2 nM. Inhibition of Notch signaling by Nirogacestat dihydrobromide while minimizing gastrointestinal toxicity presents a promising approach for research of Notch receptor-dependent cancers.

BIOLOGICAL ACTIVITY

In Vitro

The IC50 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 IC50 is determined to be 13.3 nM. Nirogacestat 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 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 is reversible[1].

SOLUBILITY

Soluble in DMSO

REFERENCES

[1]. Wei P, et al. Evaluation of selective gamma-secretase inhibitor PF-03084014 for its antitumor efficacy and gastrointestinal safety to guide optimal clinical trial design. Mol Cancer Ther. 2010 Jun;9(6):1618-28.

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