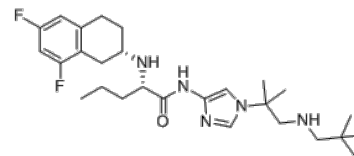


Product Name : Nirogacestat
Cat. No. : PC-49410
CAS No. : 1290543-63-3
Molecular Formula : C₂₇H₄₁F₂N₅O
Molecular Weight : 489.656
Target : γ -secretase
Solubility : 10 mM in DMSO



Biological Activity

Nirogacestat (PF-03084014) is a potent, noncompetitive, and selective gamma-secretase inhibitor, reduces amyloid-beta (Abeta) production with in vitro IC₅₀ of 1.2 nM (whole-cell assay) to 6.2 nM (cell-free assay).

PF-03084014 inhibits Notch-related T- and B-cell maturation in an in vitro thymocyte assay with an EC₅₀ of 2.1 μ M.

PF-03084014 inhibited gamma-secretase activity was shown by the reduction of endogenous Notch intracellular domain (NICD) levels and by the downregulation of Notch target genes Hes-1 and cMyc in the T-cell acute lymphoblastic leukemia (T-ALL) cell line HPB-ALL.

PF-03084014 caused cell growth inhibition of several T-ALL cell lines via cell cycle arrest and induction of apoptosis.

PF-03084014 treatment also resulted in robust NICD reduction in HBP-ALL xenograft models, exhibited broad antitumor efficacy in Notch-dependent models.

References

Lanz TA, et al. J Pharmacol Exp Ther. 2010 Jul;334(1):269-77.

Wei P, et al. Mol Cancer Ther. 2010 Jun;9(6):1618-28.

Brodney MA, et al. Bioorg Med Chem Lett. 2011 May 1;21(9):2637-40.

Samon JB, et al. Mol Cancer Ther. 2012 Jul;11(7):1565-75.

Caution: Product has not been fully validated for medical applications. Lab Use Only!

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