Product Datasheet

Avagacestat

Catalog No. **BP-02517** · CAS **1146699-66-2** · Form **free base** · Physical state **solid** · Color **White to off-white** · Version **1.0** · Revision **2026-09-10**

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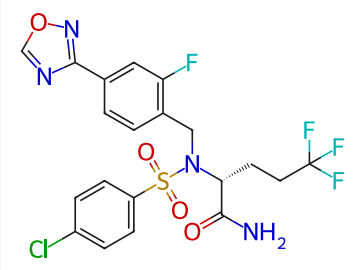
Target	Research area
γ-secretase; Notch	**Cancer**

Molecular formula	**$C_{20}H_{17}ClF_4N_4O_4S$**
Molecular weight	**520.8850**

STRUCTURE



DESCRIPTION

Avagacestat (BMS-708163) is a potent inhibitor of γ-secretase, with IC50s of 0.27 nM and 0.30 nM for Aβ42 and Aβ40 inhibition; Avagacestat (BMS-708163) also inhibits NICD (Notch IntraCellular Domain) with IC50 of 0.84 nM and shows weak inhibition of CYP2C19, with IC50 of 20 μM. Avagacestat can be used for Alzheimer disease research.

BIOLOGICAL ACTIVITY

BMS-708163 (Avagacestat) is a potent, selective γ-secretase inhibitor of Aβ40 and Aβ42 with IC50 of 0.3 nM and 0.27 nM, respectively. BMS-708163 binds directly to the presenilin-1 N-terminal fragment and that binding can be challenged by other pan-GSIs, but not by γ-secretase modulators. BMS-708163 blocks the binding of four different active site-directed GSI photoaffinity probes. Administration of a single dose of 200 or 400 mg of BMS-708163 resulted in a marked decrease in CSF Aβ(1-38), Aβ(1-40) and Aβ(1-42) concentrations vs placebo; with smaller decreases observed in the 50 mg dose group. BMS-708163 (Avagacestat) was quickly absorbed into the systemic circulation, with a mean time to reach maximum plasma concentration (t(max)) of approximately 1-2 h, and a CSF t(max) of approximately 3 h. BMS-708163 is 190-fold more selective for APP than Notch, having an IC50 of 58 nM for Notch.

SOLUBILITY

Soluble in DMSO

REFERENCES

[1].Gillman KW, et al. Letter Discovery and Evaluation of BMS-708163, a Potent, Selective and Orally Bioavailable γ-Secretase Inhibitor. Med Chem Lett, 2010, 1 (3), 120-124.

[2].Xie M, et al. γ Secretase inhibitor BMS-708163 reverses resistance to EGFR inhibitor via the PI3K/Akt pathway in lung cancer. J Cell Biochem. 2015 Jun;116(6):1019-27.

[3].Crump CJ, et al. BMS-708,163 targets presenilin and lacks notch-sparing activity. Biochemistry. 2012 Sep 18;51(37):7209-11.

[4].Borghys H, et al. A canine model to evaluate efficacy and safety of γ-secretase inhibitors and modulators. J Alzheimers Dis. 2012;28(4):809-22.

[5].Vladimir Coric, et al. Safety and tolerability of the γ-secretase inhibitor avagacestat in a phase 2 study of mild to moderate Alzheimer disease. Arch Neurol. 2012 Nov;69(11):1430-40.

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