

Avagacestat

Catalog No: tcsc0180



Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg



Specifications

CAS No:

1146699-66-2

Formula:

$C_{20}H_{17}ClF_4N_4O_4S$

Pathway:

Stem Cell/Wnt;Neuronal Signaling;Stem Cell/Wnt

Target:

γ-secretase;γ-secretase;Notch

Purity / Grade:

>98%

Solubility:

10 mM in DMSO

Alternative Names:

BMS-708163

Observed Molecular Weight:

520.89

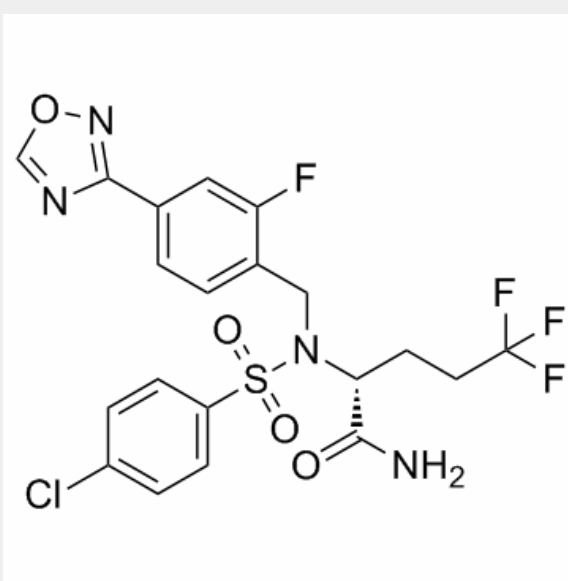
Product Description

Avagacestat (BMS-708163) is a potent inhibitor of **γ-secretase**, with **IC₅₀**s 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.

IC50 & Target: IC50: 0.27 nM (γ-secretase, Aβ₄₂), 0.30 nM (γ-secretase, Aβ₄₀), 20 μM (CYP2C19)^[1], 0.84 nM (NICD)^[2]

In Vitro: Avagacestat (BMS-708163) exhibits weaker potency for inhibition of Notch processing, IC₅₀=58±23 nM, as compared to its inhibition potency for APP cleavage^[1]. Avagacestat (BMS-708163) (10 μM) combined with gefitinib significantly attenuates the colony growth of PC9/AB2 cells, increases the expression of active caspase 3 and PARP and reduces the expression of Ki-67 in PC9/AB2 cells. Avagacestat (BMS-708163) induces apoptosis and enhances cell cycle arrest at the G1 phase in PC9/AB2 cells. Avagacestat (BMS-708163) treatment effectively downregulates the expression of Notch1, HES1, PI3K and Akt in PC9/AB2 cells^[3].

In Vivo: Avagacestat (BMS-708163) significantly reduces both plasma and brain Aβ₄₀ levels relative to control at 10 and 100 mg/kg for the entire dosing interval, demonstrates significant Aβ₄₀ lowering for 8 h after an oral dose of 1 mg/kg, and significantly lowers CSF Aβ₄₀ levels in rats, when measured 5 h after single oral doses ranging from 3 to 100 mg/kg^[1]. Avagacestat (BMS-708163) (10 mg/kg) monotherapy has a minor inhibitory effect on PC9/AB2 tumor growth compared with gefitinib alone. BMS-708163 monotherapy results in a slight increase in caspase 3 expression as well as a mild decrease in Ki-67 expression in vivo. In the xenograft lung cancer samples treated with Avagacestat (BMS-708163) plus gefitinib, there are a marked increase in caspase 3 expression and a reduction in Ki-67 staining^[3].



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