Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

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

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Avagacestat (BMS-708163) is a potent inhibitor of **γ-secretase**, with **IC_{50}**s of 0.27 nM and 0.30 nM for Aβ42 and Aβ40 inhibition; Avagacestat (BMS-708163) also inhibits NICD (Notch IntraCellular Domain) with **IC_{50}** of 0.84 nM and shows weak inhibition of CYP2C19, with IC_{50} 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, IC_{50}=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].