

# 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:**

$\gamma$ -secretase; $\gamma$ -secretase;Notch

**Purity / Grade:**

>98%

**Solubility:**

10 mM in DMSO

**Alternative Names:**

BMS-708163

**Observed Molecular Weight:**

520.89

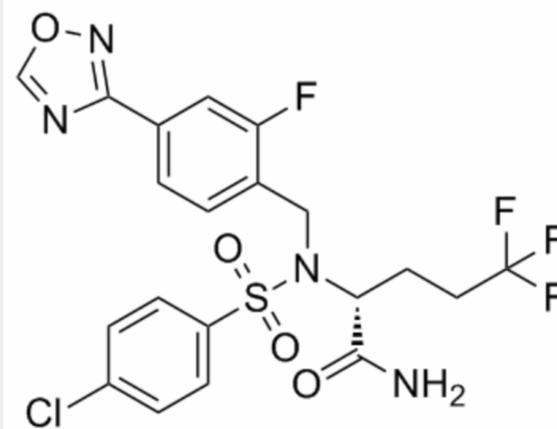
## Product Description

Avagacestat (BMS-708163) is a potent inhibitor of **γ-secretase**, with **IC<sub>50</sub>**s of 0.27 nM and 0.30 nM for Aβ<sub>42</sub> and Aβ<sub>40</sub> inhibition; Avagacestat (BMS-708163) also inhibits NICD (Notch IntraCellular Domain) with **IC<sub>50</sub>** of 0.84 nM and shows weak inhibition of CYP2C19, with IC<sub>50</sub> of 20 μM.

IC50 & Target: IC50: 0.27 nM (γ-secretase, Aβ<sub>42</sub>), 0.30 nM (γ-secretase, Aβ<sub>40</sub>), 20 μM (CYP2C19)<sup>[1]</sup>, 0.84 nM (NICD)<sup>[2]</sup>

**In Vitro:** Avagacestat (BMS-708163) exhibits weaker potency for inhibition of Notch processing, IC<sub>50</sub>=58±23 nM, as compared to its inhibition potency for APP cleavage<sup>[1]</sup>. 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<sup>[3]</sup>.

**In Vivo:** Avagacestat (BMS-708163) significantly reduces both plasma and brain Aβ<sub>40</sub> levels relative to control at 10 and 100 mg/kg for the entire dosing interval, demonstrates significant Aβ<sub>40</sub> lowering for 8 h after an oral dose of 1 mg/kg, and significantly lowers CSF Aβ<sub>40</sub> levels in rats, when measured 5 h after single oral doses ranging from 3 to 100 mg/kg<sup>[1]</sup>. 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<sup>[3]</sup>.



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!