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- Expressversand

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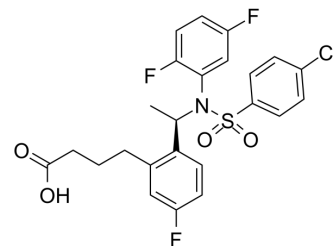
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## BMS 299897

Cat. No.:	HY-50883
CAS No.:	290315-45-6
Molecular Formula:	C <sub>24</sub> H <sub>21</sub> ClF <sub>3</sub> NO <sub>4</sub> S
Molecular Weight:	511.94
Target:	γ-secretase
Pathway:	Neuronal Signaling; Stem Cell/Wnt
Storage:	<div>Powder</div> <div>-20°C 3 years</div> <div>4°C 2 years</div> <div>In solvent</div> <div>-80°C 2 years</div> <div>-20°C 1 year</div>



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 30 mg/mL (58.60 mM)  
 \* "≥" means soluble, but saturation unknown.

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		1.9534 mL	9.7668 mL	19.5335 mL
	5 mM		0.3907 mL	1.9534 mL	3.9067 mL
	10 mM		0.1953 mL	0.9767 mL	1.9534 mL

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
 Solubility: ≥ 2.5 mg/mL (4.88 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

BMS 299897 is a sulfonamide γ-secretase inhibitor with an IC<sub>50</sub> of 7 nM for Aβ production inhibition in HEK293 cells stably overexpressing amyloid precursor protein (APP).

#### IC<sub>50</sub> & Target

IC<sub>50</sub>: 7 nM (Aβ, in HEK293 cells)<sup>[1]</sup>

#### In Vitro

BMS-299897 reduces the levels of each of the Aβ peptides. At 1 μM, BMS-299897 decreases these peptides to levels ranging from 20 to 50% of the vehicle control. BMS-299897 treatment reduces the portion of QD-BDNF signals moving in the retrograde direction (p=0.0198) with a concomitant increase in the portion of signals moving in the anterograde direction (p=0.0147)<sup>[2]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## In Vivo

BMS-299897 shows dose- and time-dependent reductions of amyloid  $\beta$ -peptide ( $A\beta$ ) in brain, cerebrospinal fluid (CSF), and plasma in young transgenic mice, with a correlation between brain and CSF  $A\beta$  levels. BMS-299897 reduces both brain and plasma  $A\beta_{1-40}$  in APP-YAC mice and increases brain concentrations of APPcarboxy-terminal fragments, consistent with  $\gamma$ -secretase inhibition. BMS-299897, attenuates this  $A\beta_{25-35}$ -induced  $A\beta_{1-42}$  seeding and toxicity. BMS-299897 is administered at 0.1-1 nmol/mouse, concomitantly with  $A\beta_{25-35}$  (9 nmol) in male Swiss mice. After one week, the contents in  $A\beta_{1-42}$  and  $A\beta_{1-40}$ , and the levels in lipid peroxidation are analyzed in the mouse hippocampus. Mice are submitted to spontaneous alternation, passive avoidance and object recognition to analyze their short- and long-term memory abilities.  $A\beta_{25-35}$  increases  $A\beta_{1-42}$  content (+240%) but fails to affect  $A\beta_{1-40}$ . BMS-299897 blocks the increase in  $A\beta_{1-42}$  content and decreased  $A\beta_{1-40}$  levels significantly. The compound does not affect  $A\beta_{25-35}$ -induced increase in hippocampal lipid peroxidation. Behaviorally, BMS-299897 blocks the  $A\beta_{25-35}$ -induced deficits in spontaneous alternation or novel object recognition, using a 1 h intertrial time interval. The co-administration of the  $\gamma$ -secretase inhibitor BMS-299897, in the 0.1-1  $\mu$ mol/mouse dose-range, completely blocks the  $A\beta_{25-35}$ -induced increase in  $A\beta_{1-42}$  content<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

### Cell Assay <sup>[2]</sup>

Neuronal cultures are treated at indicated DIVs for 24 hrs with 1  $\mu$ M BMS-299897, 2.5  $\mu$ M sGSM41 or the vehicle DMSO (final concentration: 0.1%) for most of the experiments, or for different periods of time as indicated in specific experiments. Transfections of siRNAs are performed on 100,000 neurons at DIV4 using NTER Nanoparticle transfection system following the protocol provided. The siRNAs used are: 1) siRNA against rat APP, and 2) the MISSION siRNA. Knockdown experiments are optimized by examining both mRNA and protein expression of APP. A knockdown efficiency of 80% at the mRNA level as quantitated with the 7300 Real Time PCR System and 30% at the protein level by immunoblotting is routinely achieved<sup>[2]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### Animal Administration <sup>[1]</sup>

Mice<sup>[1]</sup>

Male Swiss OF 1 mice, aged 7-9 weeks and weighing 32 $\pm$ 2 g are used. Doses of 0.1, 0.3 and 1  $\mu$ mol are injected i.c.v. in 1  $\mu$ L simultaneously with the  $A\beta_{25-35}$  peptide. Animals are used at day 7-9 after i.c.v. injections for behavioral testing or sacrifice, before biochemical measures. All experiments are conducted on separate batch of mice, except spontaneous alternation and passive avoidance, which are done in series in the same animals.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## REFERENCES

[1]. Meunier J, et al. The  $\gamma$ -secretase inhibitor 2-[(1R)-1-[(4-chlorophenyl)sulfonyl](2,5-difluorophenyl) amino]ethyl-5-fluorobenzenebutanoic acid (BMS-299897) alleviates  $A\beta_{1-42}$  seeding and short-term memory deficits in the  $A\beta_{25-35}$  mouse model of Alzheimer's d

[2]. Weissmiller AM, et al. A  $\gamma$ -secretase inhibitor, but not a  $\gamma$ -secretase modulator, induced defects in BDNF axonal trafficking and signaling: evidence for a role for APP. PLoS One. 2015 Feb 24;10(2):e0118379.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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