The γ-secretases are intramembrane cleaving protein complexes responsible for the generation of amyloid β (Aβ) from the amyloid precursor protein (APP). Apart from presenilins (PSEN), a mature and active γ-secretase complex consists of three additional subunits: Nicastrin (Nct), PSEN enhancer 2 (Pen-2), and either anterior pharynx 1 (APH-1) A or B. The γ-secretase complexes proteolyze type 1 transmembrane proteins, among them the APP, the Notch receptors and ligands, the Erb4 receptor and N-Cadherin.

Inhibition of γ-secretase with DAPT significantly reduced the production of extracellular Aβ38, Aβ40, and Aβ42 in neurons of all genotypes.

Compounds that inhibit or modulate γ-secretase can be considered as a potential therapeutics for AD because their use appears to be a rational strategy to prevent senile plaque (SP) formations.
γ-secretase Inhibitors & Modulators

Avagacestat (BMS-708163)  Cat. No.: HY-50845

Bioactivity:  Avagacestat (BMS-708163) is a potent inhibitor of γ-secretase, with IC_{50} values 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 sh...

Purity:  99.93%
Clinical Data:  Phase 2
Size:  10mM x 1mL in DMSO, 5 mg, 10 mg, 20 mg

Begacestat (GSI-953)  Cat. No.: HY-14175

Bioactivity:  Begacestat (GSI-953) is a selective thiophene sulfonamide inhibitor of amyloid precursor protein γ-secretase (IC_{50}=15 nM) for the treatment of Alzheimer’s disease.

Purity:  99.9%
Clinical Data:  No Development Reported
Size:  1 mg

BI-1408  Cat. No.: HY-112282

Bioactivity:  BI-1408 is a potent γ-secretase modulator with an IC_{50} of 0.04 μM for Aβ_{42}.

Purity:  >98%
Clinical Data:  No Development Reported
Size:  1 mg, 5 mg, 10 mg

BMS 299897  Cat. No.: HY-50883

Bioactivity:  BMS 299897 is a sulfonamide γ-secretase inhibitor with an IC_{50} of 7 nM for Aβ production inhibition in HEK293 cells stably overexpressing amyloid precursor protein (APP).

Purity:  99.35%
Clinical Data:  No Development Reported
Size:  10mM x 1mL in DMSO, 10 mg, 50 mg

Compound E (Compound E (secretase inhibitor)DuPont E)  Cat. No.: HY-14176

Bioactivity:  Compound E is a potent γ-secretase modulator. IC_{50} value: Target: γ-secretase In the present study, 9 dogs were treated with a single dose of the γ-secretase modulator E2012, the γ-secretase inhibitor LY450139, or vehicle with a dosing interval of 1 week. The isoform Aβ(1-37) was significantly...

Purity:  99.87%
Clinical Data:  No Development Reported
Size:  10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg, 25 mg

DAPT (GSI-IX)  Cat. No.: HY-13027

Bioactivity:  DAPT is a γ-secretase inhibitor with IC_{50} values of 115 and 200 nM for total Aβ and Aβ_{42}, respectively.

Purity:  99.97%
Clinical Data:  No Development Reported
Size:  10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg

E 2012  Cat. No.: HY-10016

Bioactivity:  E 2012 is a potent γ-secretase modulator. IC_{50} value: Target: γ-secretase In the present study, 9 dogs were treated with a single dose of the γ-secretase modulator E2012, the γ-secretase inhibitor LY450139, or vehicle with a dosing interval of 1 week. The isoform Aβ(1-37) was significantly...

Purity:  99.91%
Clinical Data:  No Development Reported
Size:  10mM x 1mL in DMSO, 5 mg, 10 mg, 100 mg

ELN 318463 racemate  Cat. No.: HY-50882A

Bioactivity:  ELN 318463 racemate is the racemate of ELN 318463. ELN 318463 is a selective γ-secretase inhibitor.

Purity:  >98%
Clinical Data:  No Development Reported
Size:  1 mg, 5 mg, 10 mg, 20 mg

gamma-secretase modulator 1  Cat. No.: HY-10043

Bioactivity:  γ-secretase inhibitor-1 is a γ-secretase modulator, γ-secretase inhibitor-1 is useful for Alzheimer’s disease.

Purity:  98.0%
Clinical Data:  No Development Reported
Size:  10 mg, 100 mg
gamma-secretase modulator 2
Cat. No.: HY-50754

Bioactivity: gamma-secretase modulator 2 is a potent and selective γ-secretase modulator for treatment of Alzheimer’s disease.

Purity: >98%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 10 mg, 50 mg

Itanapraced
(CHF5074; CSP-1103)
Cat. No.: HY-14399

Bioactivity: Itanapraced (CHF5074) is a novel γ-secretase modulator, reduces Aβ42 and Aβ40 secretion, with an IC50 of 3.6 and 18.4 μM, respectively.

Purity: 98.05%
Clinical Data: Phase 1
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

LY-411575
Cat. No.: HY-50752

Bioactivity: LY-411575 is a potent γ-secretase inhibitor with IC50 of 0.078 nM/0.082 nM (membrane/cell-based), and also inhibits Notch S3 cleavage with IC50 of 0.39 nM.

Purity: 98.71%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

MK-0752
Cat. No.: HY-10974

Bioactivity: MK-0752 is a moderately potent γ-secretase inhibitor, which reduces Aβ40 production with IC50 of 5 nM.

Purity: 98.87%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

gamma-secretase modulator 3
Cat. No.: HY-50889

Bioactivity: gamma-secretase modulator 3 is a γ-secretase modulator.

Purity: 98.0%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 10 mg, 100 mg

L-685458
(L-685,458)
Cat. No.: HY-19369

Bioactivity: L-685458 is a potent inhibitor of Amyloid β-Protein precursor γ-secretase activity with IC50 of 17 nM, shows greater than 50-100-fold selectivity over other aspartyl proteases tested.

Purity: 99.78%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg

LY-411575 isomer 1
Cat. No.: HY-50752A

Bioactivity: LY-411575 isomer 1 is an isomer of LY411575, which is a potent γ-secretase inhibitor.

Purity: >98%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 1 mg

LY-411575 isomer 2
Cat. No.: HY-50752B

Bioactivity: LY-411575 isomer 2 is an isomer of LY411575, which is a potent γ-secretase inhibitor.

Purity: >98%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 1 mg

LY-411575 isomer 3
Cat. No.: HY-50752C

Bioactivity: LY-411575 isomer 3 is an isomer of LY411575, which is a potent γ-secretase inhibitor.

Purity: >98%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 1 mg

LY-411575
Cat. No.: HY-50752

Bioactivity: LY-411575 isomer 1 is an isomer of LY411575, which is a potent γ-secretase inhibitor.

Purity: >98%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 1 mg

NGP555
Cat. No.: HY-108714

Bioactivity: NGP555 is a γ-secretase modulator.

Purity: >98%
Clinical Data: No Development Reported
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg
### Nirogacestat
(PF-3084014; PF-03084014)

**Bioactivity:** Nirogacestat (PF-3084014) is a reversible, noncompetitive, and selective γ-secretase inhibitor with IC\(_{50}\) of 6.2 nM.

**Purity:** 99.95%
**Clinical Data:** Phase 2
**Size:** 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

### RO4929097
(RG-4733)

**Bioactivity:** RO4929097 (RG-4733) is a γ secretase inhibitor with IC\(_{50}\) of 4 nM, inhibiting cellular processing of Aβ40 and Notch with EC\(_{50}\) of 14 nM and 5 nM, respectively.

**Purity:** 98.02%
**Clinical Data:** Phase 2
**Size:** 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

### Semagacestat
(LY450139)

**Bioactivity:** Semagacestat is a γ-secretase inhibitor, inhibits β-amyloid (Aβ42, Aβ38 and Aβ40) with IC\(_{50}\) of 10.9, 12 and 12.1 nM, respectively; also inhibits Notch signaling with IC\(_{50}\) of 14.1 nM.

**Purity:** 98.83%
**Clinical Data:** Phase 3
**Size:** 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

### Sulindac sulfide
(cis-Sulindac sulfide)

**Bioactivity:** Sulindac sulfide is a noncompetitive γ-secretase inhibitor, with an IC\(_{50}\) of 20.2 μM for γ\(_{42}\)-secretase activity.

**Purity:** >98%
**Clinical Data:** No Development Reported
**Size:** 250 mg, 500 mg

### YO-01027
(Dibenzazepine; DBZ)

**Bioactivity:** YO-01027 (Dibenzazepine;DBZ) is a potent γ-secretase inhibitor with IC\(_{50}\) values of 2.92±0.22 and 2.64±0.30 nM for Notch and APPL cleavage, respectively.

**Purity:** 99.23%
**Clinical Data:** No Development Reported
**Size:** 10mM x 1mL in DMSO, 2 mg, 5 mg, 10 mg, 25 mg

### Z-Ile-Leu-aldehyde
(Z-IL-CHO; GSI-XII; γ-Secretase inhibitor XII)

**Bioactivity:** Z-Ile-Leu-aldehyde(Z-IL-CHO; GSI-XII) is a potent gamma-Secretase inhibitor; Notch signaling inhibitor.

**Purity:** 98.10%
**Clinical Data:** No Development Reported
**Size:** 10mM x 1mL in DMSO, 5 mg, 10 mg