γ-secretase

Gamma secretase

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 proteolyse type 1 transmembrane proteins, among them the APP, the Notch receptors and ligands, the Erb4 receptor and N-Cadherin.

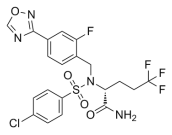
Inhibition of γ-secretase with DAPT significantly reduced the production of extracellular Aβ38, Aβ40, and Aβ42 in neurons of all genotypes.

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

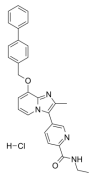


Avagacestat (BMS-708163) is a potent inhibitor of **γ-secretase**, with IC_{50}s of 0.27 nM and 0.30 nM for Aβ42 and Aβ40 inhibition; Avagacestat (BMS-708163) also inhibits NICD (Notch IntraCellular Domain) with IC_{50} of 0.84 nM and shows weak inhibition of CYP2C19, with IC_{50} of...

Purity: 99.93%
Clinical Data: Phase 2
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg

Aβ42-IN-1

Cat. No.: HY-130609

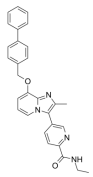


Aβ42-IN-1, compound 1v, is a novel, potent and orally active **γ-secretase modulator (GSM)**. Aβ42-IN-1 potently reduced **Aβ42** levels with an IC_{50} value of 0.091 μM without CYP3A4 inhibition. Aβ42-IN-1 shows a sustained pharmacokinetic profile.

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

Aβ42-IN-1 free base

Cat. No.: HY-130609A

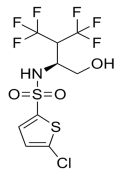


Aβ42-IN-1 free base (compound 1v) is an orally active, high brain exposure **γ-secretase** modulator. Aβ42-IN-1 free base potently reduces Aβ42 levels with an IC_{50} value of 0.091 μM, and significantly reduces brain Aβ42 levels in mice.

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

Begacestat
(GSI-953)

Cat. No.: HY-14175

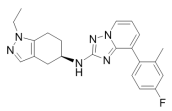


Begacestat (GSI-953) is a selective thiophene sulfonamide inhibitor of amyloid precursor protein **gamma-secretase** (IC_{50} $Aβ_{40}$=15 nM) for the treatment of Alzheimer's disease.

Purity: >99.0%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 1 mg

BI-1408

Cat. No.: HY-112282

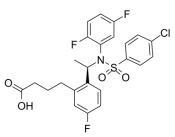


BI-1408 is a potent **γ secretase** modulator with an IC_{50} of 0.04 μM for $Aβ_{42}$.

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

BMS 299897

Cat. No.: HY-50883

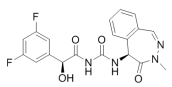


BMS 299897 is a sulfonamide **γ-secretase** inhibitor with an IC_{50} of 7 nM for Aβ production inhibition in HEK293 cells stably overexpressing amyloid precursor protein (APP).

Purity: 98.96%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

BMS 433796

Cat. No.: HY-50884

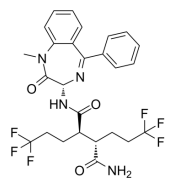


BMS 433796 is a **γ-secretase** inhibitor with **Aβ** lowering activity in a transgenic mouse model of Alzheimer's disease.

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

BMS-906024

Cat. No.: HY-15670

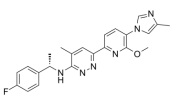


BMS-906024 is an oral and selective **gamma secretase** inhibitor. BMS-906024 is a potent pan-**Notch** receptors inhibitor with IC_{50}s of 1.6 nM, 0.7 nM, 3.4 nM, and 2.9 nM for Notch1, -2, -3, and -4 receptors, respectively.

Purity: >98%
Clinical Data: Phase 1
Size: 1 mg, 5 mg

BPN-15606

Cat. No.: HY-117482

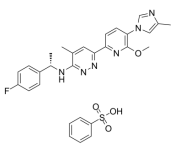


BPN-15606 is a highly potent, orally active **γ-secretase** modulator (GSM), attenuates the production of **Aβ42** and **Aβ40** by SHSY5Y neuroblastoma cells with IC_{50} values of 7 nM and 17nM, respectively.

Purity: 99.24%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg

BPN-15606 besylate

Cat. No.: HY-117482A



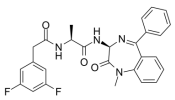
BPN-15606 besylate is a highly potent, orally active **γ-secretase** modulator (GSM), attenuates the production of **Aβ42** and **Aβ40** by SHSY5Y neuroblastoma cells with IC_{50} values of 7 nM and 17nM, respectively.

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

Compound E

Cat. No.: HY-14176

Compound E is a **γ-secretase** inhibitor. Compound E bloks β-amyloid(40), β-amyloid(42), and Notch γ-secretase cleavage with IC_{50}s of 0.24, 0.37, 0.32 nM, respectively.



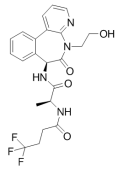
Purity: 99.87%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 1 mg, 5 mg, 10 mg, 25 mg

Crenigacestat

(LY3039478)

Cat. No.: HY-12449

Crenigacestat is an orally active **Notch** and **γ-secretase** inhibitor, with an IC_{50} of 1nM in most of the tumor cell lines tested.



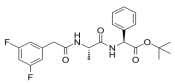
Purity: 98.62%
Clinical Data: Phase 2
Size: 10 mM × 1 mL, 2 mg, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

DAPT

(GSI-IX)

Cat. No.: HY-13027

DAPT (GSI-IX) is a potent and orally active **γ-secretase** inhibitor with IC_{50}s of 115 nM and 200 nM for total **amyloid-β (Aβ)** and $Aβ_{42}$, respectively. DAPT inhibits the activation of **Notch 1** signaling and induces cell differentiation.

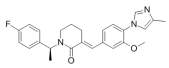


Purity: 99.97%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg

E 2012

Cat. No.: HY-10016

E 2012 is a potent **gamma (γ) secretase** modulator without affecting Notch processing. E 2012 inhibits 3β-hydroxysterol Δ24-reductase **(DHCR24)** at the final step in the cholesterol biosynthesis.

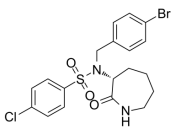


Purity: 96.91%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 5 mg, 10 mg, 100 mg

ELN318463

Cat. No.: HY-50882

ELN318463 is an amyloid precursor protein (APP) selective **γ-secretase** inhibitor. ELN318463 shows differential inhibition of presenilin (PS1)- and PS2-comprised γ-secretase with EC_{50}s of 12 nM and 656 nM for PS1 and PS2, respectively. ELN318463 is 51-fold more selective for PS1.

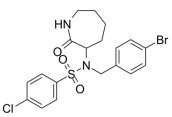


Purity: >98%
Clinical Data: No Development Reported
Size: 5 mg, 10 mg, 50 mg, 100 mg

ELN318463 racemate

Cat. No.: HY-50882A

ELN318463 racemate is the racemate of ELN318463. ELN318463 is an amyloid precursor protein (APP) selective **γ-secretase** inhibitor. ELN318463 shows differential inhibition of presenilin (PS1)- and PS2-comprised γ-secretase with EC_{50}s of 12nM and 656 nM for PS1and PS2, respectively.

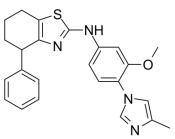


Purity: >98%
Clinical Data: No Development Reported
Size: 1 mg, 5 mg

gamma-secretase modulator 1

Cat. No.: HY-10043

γ-secretase inhibitior-1 is a gamma-secretase modulator, γ-secretase inhibitior-1 is useful for Alzheimer's disease.

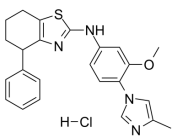


Purity: >98.0%
Clinical Data: No Development Reported
Size: 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

gamma-secretase modulator 1 hydrochloride

Cat. No.: HY-10043A

gamma-secretase inhibitior-1 is a **gamma-secretase** modulator, γ-secretase inhibitior-1 is useful for Alzheimer's disease.

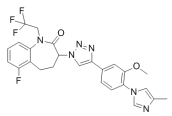


Purity: 98.59%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

gamma-secretase modulator 2

Cat. No.: HY-50754

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

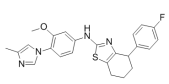


Purity: 98.59%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 10 mg, 50 mg

gamma-secretase modulator 3

Cat. No.: HY-50889

gamma-secretase modulator 3 is a gamma-secretase modulator.

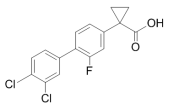


Purity: 99.35%
Clinical Data: No Development Reported
Size: 10 mg, 100 mg

Itanapraced

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

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

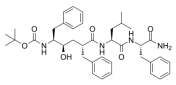


Purity: >98.0%
Clinical Data: Phase 1
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg

L-685458

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

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. IC50 value: 17 nM Target: γ-secretase in vitro: L-685458 is a Notch inhibitor.

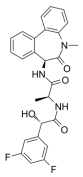


Purity: 99.78%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 1 mg, 5 mg, 10 mg

LY-411575

Cat. No.: HY-50752

LY-411575 is a potent **γ-secretase** inhibitor with IC_{50} of 0.078 nM/0.082 nM (membrane/cell-based), and also inhibits Notch S3 cleavage with IC_{50} of 0.39 nM.

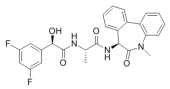


Purity: 99.20%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg

LY-411575 isomer 1

Cat. No.: HY-50752A

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

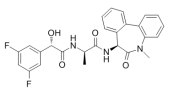


Purity: 99.51%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 1 mg

LY-411575 isomer 2

Cat. No.: HY-50752B

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

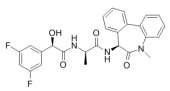


Purity: 99.84%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 1 mg

LY-411575 isomer 3

Cat. No.: HY-50752C

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

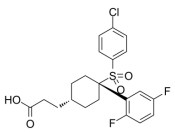


Purity: 99.27%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 1 mg

MK-0752

Cat. No.: HY-10974

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

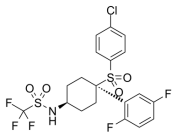


Purity: 98.00%
Clinical Data: Phase 2
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg

MRK-560

Cat. No.: HY-14174

MRK-560 is a potent, orally bioavailable and brain-penetrant **γ-secretase** inhibitor.

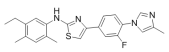


Purity: >99.0%
Clinical Data: No Development Reported
Size: 5 mg

NGP555

Cat. No.: HY-108714

NGP555 is a **γ-secretase** modulator.

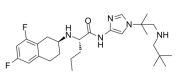


Purity: 98.64%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

Nirogacestat

(PF-3084014; PF-03084014) Cat. No.: HY-15185

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

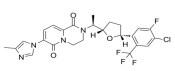


Purity: 99.95%
Clinical Data: Phase 2
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg

PF-06648671

Cat. No.: HY-120789

PF-06648671 is a novel, brainpenetrable, and orally active **γsecretase modulator (GSM)**. PF-06648671 reduces Aβ42 and Aβ40, with concomitant increases in Aβ37 and Aβ38 in vitro. PF-06648671 is used for the study of Alzheimer's disease.</br>.



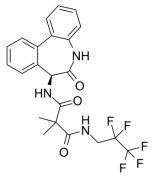
Purity: >98%
Clinical Data: No Development Reported
Size: 1 mg, 5 mg

RO4929097

(RG-4733)

Cat. No.: HY-11102

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.



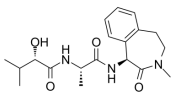
Purity: 98.29%
Clinical Data: Phase 2
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg

Semagacestat

(LY450139)

Cat. No.: HY-10009

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.



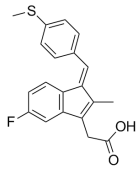
Purity: 98.83%
Clinical Data: Phase 3
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg

Sulindac sulfide

(cis-Sulindac sulfide)

Cat. No.: HY-B1786

Sulindac sulfide is a noncompetitive **γ-secretase** inhibitor, with an IC_{50} of 20.2 μM for γ_{42}-secretase activity.



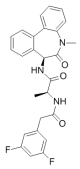
Purity: >98%
Clinical Data: No Development Reported
Size: 1 mg, 5 mg

YO-01027

(Dibenzazepine; DBZ)

Cat. No.: HY-13526

YO-01027 (Dibenzazepine;DBZ) is a potent **γ-secretase** inhibitor with IC_{50} values of 2.92 and 2.64 nM for **Notch** and **APPL** cleavage, respectively.



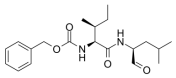
Purity: 99.23%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 2 mg, 5 mg, 10 mg, 25 mg

Z-Ile-Leu-aldehyde

(Z-IL-CHO; GSI-XII; γ-Secretase inhibitor XII)

Cat. No.: HY-12465

Z-Ile-Leu-aldehyde (Z-IL-CHO) is a potent and competitive peptide aldehyde inhibitor of **γ-secretase** and **notch**.

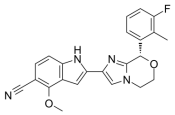


Purity: 98.10%
Clinical Data: No Development Reported
Size: 10 mM × 1 mL, 5 mg, 10 mg

γ-Secretase modulator 4

Cat. No.: HY-128581

γ-Secretase modulator 4 is a potent **γ-secretase** modulator, reduces the Aβ42 level with IC_{50}s of 0.014 μM and 0.017 μM in human and mouse, respectively.



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