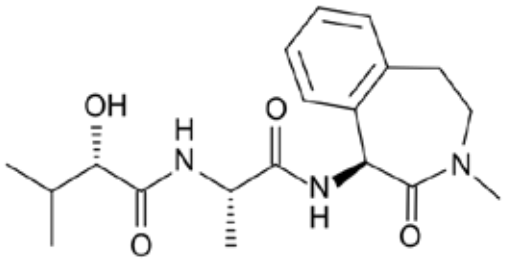
γ-Secretase Inhibitors

γ-Secretase is a multi-subunit protein responsible for cleaving transmembrane proteins such as amyloid precursor protein and Notch. Cleavage of amyloid precursor protein eventually results in the formation of amyloid-β, the main component of amyloid plaques characteristic of Alzheimer's disease[1]. Cleavage of Notch allows for gene transcription and other downstream signal transduction necessary for cell-cell communications involved in embryogenesis, cell differentiation, endocrine development, and potentially tumorigenesis[2]. Notch activity promotes cell survival and suppresses apoptosis.

Available inhibitors:
D0260 DAPT
D1773 Deshydroxy LY-411575
F4432 FLI-06
L9701 LY-450139
M4200 MK-0752



L9701 LY-450139

Inhibition of γ-secretase and Notch signaling can decrease production of amyloid-β peptides and halt or slow cell division, particularly for stem cells. Inhibition of Notch signaling appears to target cancer stem cells, stopping growth and inducing differentiation or apoptosis[3]. Because Notch interacts with many other signaling pathways and components such as PI3K/Akt, Ras, NF-kB, EGFR, and VEGFR, these downstream targets are affected as well.

LKT Laboratories carries several γ-secretase inhibitors that exhibit activity in a variety of research applications. In animal models of Alzheimer's disease, **LY-450139 (L9701)** prevents production of new amyloid plaques[4]. **MK-0752 (M4200)** displays potential as a treatment for brain and CNS-centric cancers[5-6]. **FLI-06 (F4432)** inhibits protein secretion prior to endoplasmic reticulum exit, exhibiting neuroprotective benefit[7].

References:
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3. Purow B. Adv Exp Med Biol. 2012; 727: 305–319.
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5. Olson RE, Albright CF. Curr Top Med Chem. 2008;8(1):17-33.
6. Hoffman LM, Fouladi M, Olson J, et al. 2015 Aug;31(8):1283-9.
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