

IMS-P15 **Discovery of a Novel and Potent γ -Secretase Modulator, E2012, for the Treatment of Alzheimer's Disease**

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To discover novel γ -secretase modulator (GSM), which is structurally different from NSAID derivatives, cell-based HTS was executed by measurement of amyloid beta 42 (A β 42) followed by characterization as a GSM. Among several structural classes identified from the HTS, phenyl imidazole derivatives were selected as a lead compound series through multiple drug-likeness assessments. The optimization process with systematic SAR investigation finally led to a clinical candidate (E2012), which demonstrates robust reduction of A β 42 in plasma, CSF and brain. In this presentation, the discovery process and profile of E2012 will be highlighted.