BDNF Small Molecule Agonists

FCUS BIOMOLECULES

Brain-derived neurotrophic factor (BDNF) along with its high affinity receptor, tropomyosin-receptor-kinase B (TrkB) play central roles in neuronal differentiation, synapse plasticity, and memory. BDNF itself has limited clinical utility. Small molecules that mimic BDNF's neurotrophic activity may offer greater therapeutic potential.¹ Recently several new BDNF mimetics and related compounds have been identified and are described below.

LM22A-4

A potent TrkB partial agonist (IC₅₀=47 nM) which induces the activation of Trk, Akt and ERK in mouse hippocampus and striatum. It improves motor learning after traumatic brain injury in rats² and restores biochemical and functional abnormalities in mouse models.³

Product No: 10-1405 5 mg/ 25 mg/

AS-1949490

A potent and selective inhibitor of the intracellular phosphatase SHIP2 (SH2 domain-containing inositol 5'-phosphatase 2), $IC_{50} = 0.62 \ \mu M$. Displays ca. 30-fold selectivity for SHIP2 over SHIP1. Activates insulin signaling via the Akt pathway in liver and lowers glucose levels in diabetic mice. Enhances BDNF expression in cultured cortical neurons.⁴

Product No: 10-5103 5 mg/ 25 mg/

FTY720 HCI

FTY720 (Fingolimod) is a selective sphingosine-1-phosphate receptor agonist. It increases BDNF levels and improves symptoms in a mouse model of RETTs syndrome. It promotes the neuroprotective effects of microglia and upregulates production of glial cell-derived neurotrophic factor as well as BDNF.⁵

Product No: 10-2138 50 mg/ 250 mg/

Auraptene

A bioactive terpenoid occurring in a variety of citrus fruits and possessing therapeutic potential. Displays neuritogenic activity and neuroprotective effects via suppression of inflammation and induction of GDNF and BDNF in neuronal cells.⁶

Product No: 10-2593 10 mg/ 50 mg/

LM11A-31

Novel nonpeptidyl p75^{NTR} ligand which induces survival signaling, inhibits pro-NGF-induced death⁷, protects neurogenesis after traumatic brain injury, promotes myelin sparing and functional recovery after spinal cord injury and reverses cholinergic neurite dystrophy in Alzheimer's disease mouse models.

Product No: 10-1526

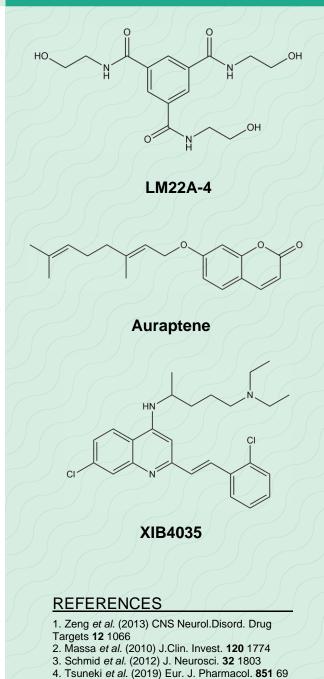
<u>5 mg/ 25 mg/</u>

XIB4035

Novel small molecule nonpeptidyl agonist at the GDNF family receptor alpha-1 (GFRα1). It induces Ret autophosphorylation in Neuro-2A cells and promotes neurite outgrowth in a concentration-dependent manner.⁸

Product No: 10-1486_____

<u>_5 mg/ 25 mg/</u>



- 5. Noda *et al.* (2013) J. Neuroimmunol. **256** 13
- 6. Furukawa *et al.* (2020) Molecules **25** 1117
- 7. Massa *et al.* (2006) J. Neurosci. **26** 5288
- 8. Drinkut et al. (2016) Cell Death Dis. 7 e2359

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