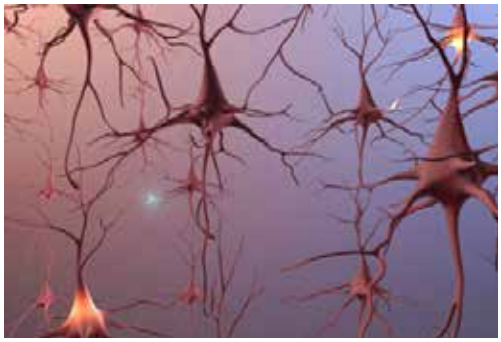
Bexarotene

Bexarotene (B1992) is a retinoid specifically selective for retinoid X receptors (RXRs). Bexarotene is a chemotherapeutic agent in the treatment of cutaneous T cell lymphoma. Research also suggests that bexarotene exhibits potential biological activity in the treatment of Alzheimer's disease as well.

The correlation between amyloid-β plaques and Alzheimer's disease is well established[1]. The accumulation and aggregation of misfolded plaques interferes with neuronal function and neurotransmission by inhibiting the transfer of signals in the brain. Amyloid-β peptides are produced by cleavage of amyloid precursor protein (APP), a transmembrane glycoprotein. Although the normal functions of amyloid-β are not well understood, it is primarily aggregation of the misfolded fragments that is linked to the development of Alzheimer's disease.

Apolipoprotein E is a protein that is responsible for facilitating the clearance of amyloid-β plaques. Transcriptional activation of apolipoprotein E is normally induced through activity at nuclear receptors such as RXRs. Bexarotene, as an RXR agonist, enhances the clearance of soluble amyloid-β within hours of administration in animal models of Alzheimer's disease[2]. Amyloid-β plaque area is reduced by more than 50% within three days. Bexarotene also stimulates the reversal of cognitive deficits and improves neural ciruit function.



Healthy neurons

Neurons surrounded by amyloid-β plaques

Further research with bexarotene examining its activity in Alzheimer's disease models and other research applications is ongoing. As RXR activation stimulates physiological amyloid-β clearance mechanisms, bexarotene and other RAR agonists such as **9-cis-Retinoic Acid (R1777)** and **13-cis-Retinoic Acid (R1779)** may gain new relevance in neurodegenerative disease studies.

References:
1. Tiraboschi P, Hansen LA, Thal LJ, et al. Neurology. 2004 Jun 8;62(11):1984-9.
2. Cramer P, Cirrito J, Wesson DW, et al. Science. 2012 Mar 23;335(6075):1503-6.