



Small peptide inhibitors of beta-amyloid toxicity

Development status

Drug discovery

▶ Pre-clinical

Phase I.

Phase II.

Phase III.

IP status

In priority year

PCT I.

PCT II.

▶ National/regional phase

Validation

Challenge

Alzheimer' disease (AD) is the most common form of dementia. There is no cure for the disease, which worsens as it progresses, and eventually leads to death. Although Alzheimer's disease develops differently for every individual, there are many symptoms. The cause and progression of AD are not well understood. Research indicates that the disease is associated with plaques and tangles in the brain. Current treatment only helps with the symptoms of the disease. There is no available treatment that stops or reverses the progression of the disease.

Technology

A new group of short peptides and peptidomimetics is described in this invention. The rational drug design approach started with statistical bioinformatical analysis of amino acid sequences of proteins binding to β -amyloid. The common A β -binding sequences were synthesized and screened in vitro (MTT-assay in SH-SY5Y cell culture) for selecting a hit compound. As a second step a lead compound was chosen after docking a series of peptides and peptidomimetics to A β oligomers simulating molecular interactions. Lead optimization was performed with synthesis of 65 novel compounds and screened with in vitro /ex vivo (MTT assay in acute rat hippocampal slices) and in vivo methods (rat one-cell electrophysiology). Two compounds (BFR 106 and BZSPB1) were chosen from the 65-membered cohort for further drug development.

Based on these experimental data the reported compounds BFR-106 and BZSPB-1 are potent neuroprotective agents counteracting the toxic effect of A β 1-42 oligomers both in vitro and in

vivo. These early-phase compounds could be therefore considered as drug candidates for neuroprotection in AD.

Keywords

neurodegenerative disease, Alzheimer's disease, β – amiloid, peptidomimetics

Benefits

- ▶ This invention relates to the field of therapeutic peptides and peptidomimetics for reducing the neurotoxicity of β – amiloid or amyloid – like protein aggregates and developing treatments for neurodegenerative disease, particularly Alzheimer's disease, in which there is accumulation of misfolded and/or aggregated proteins.
- ▶ Our strategy is to design inhibitory peptides and peptidomimetics of various types and conformations that bind in the A β molecule by weak interaction but due to the hydrophobic interaction with toxic A β -oligomers they prompt their rapid sequestration to larger nontoxic A β – aggregates.

Development status

On the basis of the promising preliminary results, the goal is to develop the preclinical dossier, complete investigations and launch phase 1 clinical trials. The exact mechanism of action is currently being investigated. Plans include further investigations of the compound in all the other models of neurodegenerative diseases.

IP status

PCT examination was submitted in 2014 (PCT/HU2014/000042). The PCT examination was extended to a Hungarian patent application (P1600222).

What we are looking for

The University of Szeged is looking for partners to develop the exact mechanism of action and to start ADME/Tox studies to complete the pre-clinical dossier.

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