# *Media release*





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## Breakthrough approach to the management of amyloidosis

### Important implications for Alzheimer's disease and diabetes



A major scientific breakthrough in the understanding of amyloid metabolism and a description of a new approach to reducing amyloid deposits was announced by a collaboration of Roche scientists, Professor Mark Pepys, the lead investigator from the Royal Free University College of Medicine (London), and other university centers. Amyloid deposits are a contributor to the development of amyloid-related conditions, such as Alzheimer's Disease, type II diabetes and organ failure. The discovery, published in the May 16 issue of Nature, is the first known example of a low molecular weight drug that rapidly reduces levels of a specific plasma protein enabling amyloid regression from both the circulation and body tissues.

"Amyloid (protein) deposits are linked to clinical tissue dysfunction in a number of areas, such as Alzheimer's disease and type II diabetes and organ failure," said Andrew Sleight, Ph.D., head of Preclinical Central Nervous System (CNS) research at Roche in Basel, Switzerland. "Therefore, new treatments, designed to promote the removal of these damaging deposits, are urgently needed to manage the accumulation of these deposits in the body (amyloidosis) and to verify the role of amyloid in these wide-spread medical conditions."

The paper summarizes animal studies and an early clinical trial of a new drug, known as CPHPC, that rapidly lowers blood levels of a normal plasma protein called serum amyloid P component (SAP). The compound was prepared by Roche chemists in the course of an extensive optimization program based on a lead structure identified by screening of the Roche compound library. CPHPC was selected as the optimal candidate for clinical proof of concept studies.

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### SAP and amyloid deposits

SAP is found in amyloid deposits of all origin. It is a very stable protein and can only be degraded by the liver. SAP is believed to stabilize the amyloid and protect it from being degraded by the body.

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Amyloid deposition leads to structural and functional damage to the tissue, which finally results in organ dysfunction and death. "CPHPC competitively inhibits the binding of SAP to these amyloid fibrils and also cross-links and binds multiple SAP molecules. This action results in the rapid removal of SAP from the circulation and the depletion of SAP from amyloid deposits in human tissues," added Sleight. "Depletion of a specific plasma protein from the circulation and the tissues by a small molecular weight compound is a completely new mechanism of drug action." Amyloid deposits are a hallmark of amyloidosis, a fatal condition that affects a wide range of organ systems such as nerve degeneration in Alzheimer's Disease, which affects about 10 million people worldwide, and islet cell failure in type II diabetes, which affects approximately six percent of the population.

"Profound depletion of SAP from blood plasma dramatically shifts the distribution of SAP between plasma and amyloid pools," said Roland Jakob-Roetne, Ph.D., Roche research leader on the SAP project. "We hope to prove, with ongoing studies, that the efficient removal of SAP will reduce the stability of amyloid plaques, promote their spontaneous regression in the body and also slow the development of new amyloid plaque in patients."

**About amyloidosis**

Amyloidosis is a disorder in which normal proteins somehow fold themselves into a form that is unusable by the human body. These proteins are deposited in tissues as abnormal and insoluble fibrils, leading to tissue damage and disease. Treatments that reduce the amount of fibril precursor proteins can lead to a regression of amyloid deposits. Amyloidosis is responsible for one of every thousand deaths in developed countries worldwide.

**CNS research at Roche**

Roche currently has 138 projects in research and 74 in development, including 48 new molecular entities (NMEs). This represents a 35% increase in the number of NMEs in our development portfolio over the past 12 months. In CNS research, Roche scientists are focused on identifying and developing new treatments for a wide range of conditions such as Alzheimer's Disease, schizophrenia, depression and anxiety. One of latest compounds to enter trials in humans is R673, an NK-1 receptor antagonist. This compound could represent a new generation of anti-depressant, offering patients the advantage of good efficacy with fewer adverse effects than the previous generation of drugs. Roche recently announced the expansion of its collaboration with Vernalis, which will now focus on the discovery and development of drugs for depression and anxiety.

**About Roche**

Headquartered in Basel, Switzerland, Roche (www.roche.com) is one of the world's leading research-oriented healthcare groups in the fields of pharmaceuticals, diagnostics and vitamins. Roche's products and services address prevention, diagnosis and treatment of diseases, thus enhancing well-being and quality of life. Roche has approximately 64,000 employees and sells its products in over 170 countries. Research at Roche focuses on significant unmet medical needs in the management of diseases of the central nervous system and genitourinary tract, metabolic disorders, inflammation, bone diseases, cancer, vascular diseases and virology.