

**Debiopharm S.A. starts a phase II trial for a once daily oral formulation of ZT-1 to treat Alzheimer's disease**

Lausanne, Switzerland - Debiopharm S.A. (Debiopharm) reported today that it will start a phase II trial this year, for dose-finding and efficacy assessment of a once daily oral formulation of ZT-1, a novel cholinesterase inhibitor, currently under development at Debiopharm for the treatment of Alzheimer's disease (AD). The multicentre trial will be conducted in France, Belgium and Switzerland, and will enroll 180 patients suffering from mild to moderate AD.

ZT-1's dual pharmacological mechanism of action offers the potential to slow deterioration, while improving cognitive function. In addition to its established anti-acetylcholinesterase (AChE) activity, ZT-1 has neuroprotective properties, one of them being mediated possibly by the N-methyl-D-aspartate (NMDA) receptor.

Alzheimer's disease is characterised by the degeneration of the neurones responsible for the synthesis of acetylcholine (ACh), a neurotransmitter with a central role in memory and other mental functions. Currently, the only available treatment for AD in most countries has been the administration of cholinesterase inhibitors, which increase the amount of ACh at the neuronal synaptic cleft by inhibiting acetylcholinesterase (AChE), the enzyme responsible for the breakdown of ACh. After oral administration, ZT-1 is progressively hydrolysed into the active compound huperzine A (hup A). Hup A is one of the most potent AChE inhibitors and was originally isolated by Chinese scientists from the club moss *Huperzia serrata*. Debiopharm is currently developing an injectable sustained-release formulation of ZT-1. The pharmacokinetic results in animals showed a stable release pattern over several weeks. This confers the potential to further benefit AD patients due to improved compliance and a close medical follow-up with monthly injections.

Pr. J.-M. Orgogozo, Professor of Neurology at the University Hospital of Bordeaux, France, and coordinator of the trial, said "There is room for improvement for this class of drugs, both for efficacy and for tolerance. This study will be important for the future management of AD patients." Professor Orgogozo was present at the 7th Annual French Meeting on Alzheimer's disease organized by the French Geriatrics and Gerontology Society in Paris, where the investigators' meeting was held.

AD is the most common form of dementia affecting elderly people, with a mean duration of around 8.5 years between the onset of clinical symptoms and death. The incidence of AD increases with age, even in the oldest age groups: from 0.5% at 65, it rises to nearly 8% at 85 years of age. Women probably have a higher risk of developing dementia than men, especially at very old ages. Worldwide, some 12 million individuals have AD and by 2025 that number is expected to increase to 22 million.

About Debiopharm S.A.

Debiopharm, Debio R.P. and Debioclinic are an established and proven group of three synergistic and complementary companies, that have a successful track record in developing, registering and ensuring that new chemical entities are brought to market both in Europe and in the United States.