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### **FOR IMMEDIATE RELEASE**

#### **DEBIOPHARM S.A. PRESENTS RESULTS OF A FIRST MONTHLY INJECTABLE SUSTAINED-RELEASE FORMULATION OF ZT-1 FOR ALZHEIMER'S DISEASE**

Lausanne, Switzerland, November 6, 2003 – Today, at the 4<sup>th</sup> Neurobiology of Aging Conference in New Orleans, USA, Debiopharm S.A. (Debiopharm) presented the results of an *in vivo* evaluation in rats of an injectable once-monthly sustained-release formulation of ZT-1. This is the first sustained-release formulation to be developed for the treatment of Alzheimer's disease (AD). After oral or parenteral administration, ZT-1 is progressively hydrolysed into the active compound huperzine A (hup A). Hup A is one of the most potent acetylcholinesterase (AChE) inhibitors. One of the current limitations of this therapeutic class of drugs is that the oral route results in variability of exposure, as well as in difficulty of compliance, especially by patients affected with this particular disease. The results of the animal study suggest that, in addition to its action in inhibiting cholinesterases, the sustained-release formulation of ZT-1 could confer advantageous neuroprotective properties to the molecule. The potential for neuroprotection of hup A is documented in different animal models and Debiopharm will evaluate this effect clinically.

Dr. R.-Y. Mauvernay, President and CEO of Debiopharm said, "It is the first time an injectable sustained-release formulation of a drug is being developed for patients suffering from AD. We have taken on this challenge as it offers a real benefit to AD patients. We believe that improved compliance will actually result in a more efficacious drug. The sustained-release formulation of ZT-1 is produced by Debio RP, a world leader in polylactide-coglycolide (PLGA) platform technology. Debio RP has already developed two other sustained-release PLGA products, both approved by the American FDA and market leaders in their therapeutic area."

Debiopharm is also studying an oral formulation of ZT-1 and will run a Phase II multi-centre trial in France, Belgium and Switzerland with 180 patients suffering from mild to moderate AD.

AD is characterised by the degeneration of the neurons responsible for the synthesis of acetylcholine (ACh), a neurotransmitter with a central role in memory and other mental functions. Current treatment for AD in most countries consists in the administration of cholinesterase inhibitors, which increase the amount of ACh at the neuronal synaptic cleft by inhibiting AChE, the enzyme responsible for the breakdown of ACh. 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. Products successfully registered and launched include oxaliplatin for advanced colorectal cancer and triptorelin pamoate for prostate cancer, both market leaders in their therapeutic areas. Specialized in oncology, hormonal and niche products for serious medical conditions, Debiopharm is a partner of research institutions, pharmaceutical and biotechnology companies who seek to develop and register their drugs. Debio R.P., Debiopharm's sister company, is a leading world player in the research, development and manufacturing of polymer-based controlled release injectable formulations for peptides and proteins, including proprietary technologies suitable for other therapeutic modalities such as soluble polymer cytotoxic-drug conjugates for parenteral administration. Debio R.P. also carries out scale-up under current good manufacturing practice (cGMP) and has an FDA-inspected plant. Debioclinic, the third Debio company, is a contract research organisation fully dedicated to clinical development. For more information, please visit the Debiopharm website at [www.debio.com](http://www.debio.com).

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