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**Results of Phase II / III Studies of Rivastigmine Patch, the World's First Transdermal Therapy for Alzheimer's Disease, Were Presented at OCAD**

Novartis, Switzerland corporation, released Phase II / III data for rivastigmine (trade name overseas: Exelon<sup>®</sup>) patch, the company's world's first transdermal therapy for Alzheimer's disease under development, at the 10<sup>th</sup> International Conference on Alzheimer's Disease and Related Disorders (ICAD) held on July 15<sup>th</sup> through 20<sup>th</sup> in Madrid, Spain. Attached for your information is the press release that Novartis issued pertaining to the study results.

In Japan, rivastigmine patch has been developed by Novartis Pharma K.K. so far. In accordance with the licensing agreement between Novartis and Ono Pharmaceutical Co., Ltd., signed in December 2005, the product will be co-developed by Novartis Pharma K.K. and Ono.

Novartis Pharma K.K. has completed early Phase II studies in Japan, and both companies are currently under preparation for late Phase II studies.

**MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG****EMBARGOED FOR RELEASE UNTIL JULY 19, 2006, 4.00 PM (CET TIME)****Exelon® Patch, the first transdermal therapy for Alzheimer's disease, may provide promising new approach to treatment of dementia**

- *IDEAL study shows potential of once-daily Exelon Patch for improving memory and maintaining everyday activities of Alzheimer's patients*
- *Over 70% of caregivers preferred patches to capsules due to better compliance and less interference with daily lives*
- *Alzheimer's disease the most common form of dementia, affects an estimated 15 million people worldwide*

**Basel, July 19, 2006** – An international study of the first transdermal patch for patients with Alzheimer's – a degenerative brain disease estimated to affect more than 15 million people worldwide – has shown that it may provide a promising new treatment approach<sup>1</sup>.

The six-month IDEAL trial of 1,195 patients with Alzheimer's disease showed that the Exelon® Patch provided benefits across a range of symptoms and the target dose was well tolerated. Results were presented today at the 10<sup>th</sup> International Conference on Alzheimer's Disease and Related Disorders (ICAD), presented by the Alzheimer's Association in Madrid, Spain.

Patients receiving Exelon Patch (rivastigmine transdermal patch) had significant improvements in memory and were better able to maintain everyday activities<sup>1</sup> than those receiving placebo. They could also complete a concentration task up to 20 seconds faster compared to those taking placebo, and physicians considered Exelon Patch patients to have done better overall.

In addition, over 70% of caregivers in the IDEAL study preferred the patch to capsules as a method of drug delivery for reasons including helping them follow the treatment schedule, overall ease of use and less interference with daily life<sup>2</sup>, according to a questionnaire in the study.

“The patch represents an important new option for people with Alzheimer's disease and their families,” said lead study investigator Professor Bengt Winblad of the Karolinska Institute in Stockholm, Sweden. “The target rivastigmine patch dose provided similar efficacy to that

achieved at the highest doses of the capsule with three times fewer reports of nausea and vomiting. A transdermal patch may prove to be the best way to deliver rivastigmine to treat Alzheimer's."

Transdermal patches are designed to provide controlled, continuous delivery of drug through the skin. This maintains steady drug levels in the bloodstream, which may reduce side effects and consequently allow access to higher doses. In addition, patches may help caregivers to monitor treatment compliance because they provide visual reassurance that the medication has been taken.

"Although Alzheimer's disease treatments have been available in oral forms for some time, we believe a patch may offer unique advantages for patients with this condition," said James Shannon, MD, Global Head of Development at Novartis Pharma AG. "If approved, the Exelon Patch could potentially improve therapy compliance and help patients and their caregivers in reaching a better quality of life."

Exelon is a cholinesterase inhibitor already approved in many countries for the treatment of mild to moderate Alzheimer's disease and dementia associated with Parkinson's disease. The IDEAL results will support the regulatory submission of the Exelon Patch to health authorities, planned by the end of 2006.

### **About the IDEAL study**

IDEAL (Investigation of Transdermal Exelon in Alzheimer's disease) was a 24-week, multi-center, randomized, double-blind, placebo- and active-controlled trial to compare the efficacy, safety and tolerability of the once-daily Exelon Patch with conventional twice-daily Exelon capsules in patients with moderate Alzheimer's disease. The primary outcomes measures were the Alzheimer's Disease Assessment Scale – cognitive subscale (ADAS-cog) and Alzheimer's Disease Cooperative Study - Clinical Global Impression of Change (ADSC-CGIC).

IDEAL was conducted in 21 countries and involved 100 centers and 1,195 patients aged 50-85 years old with a score of 10-20 in the Mini-Mental State Examination (MMSE), the most widely-used test for assessing memory problems or dementia. Patients received Exelon either in capsules (6 mg twice-daily) or patches in two sizes, namely Patch 10 (providing 9.5 mg over 24 hours) or Patch 20 (17.4 mg/24 h)<sup>1</sup>.

Both patch sizes showed superior efficacy to placebo. The target dose of Patch 10 showed similar efficacy to the highest doses of Exelon capsules with three times fewer reports of nausea (7.2 percent vs. 23.1 percent) and vomiting (6.2 percent vs. 17.0 percent), which are well-known side effects of cholinesterase inhibitors. Patch 20 showed numerically but not statistically improved cognitive scores versus capsules and similar tolerability to capsules.

Local skin tolerability was good. The percentage of patients who reported moderate or severe redness of the skin at any point of the study was only 7.6 percent and 6.2 percent of patients receiving Patch 10 and 20, respectively. The patch also demonstrated very good skin adhesion over 24 hours in a range of everyday situations such as bathing and in hot weather.

### **About Exelon**

Since 1997, Exelon (rivastigmine tartrate) has been widely used to treat mild to moderate Alzheimer's disease in more than 70 countries. Exelon is the only cholinesterase inhibitor to be also approved to treat both Alzheimer's disease and dementia associated with Parkinson's disease (PDD) in Europe and US.

Exelon belongs to a class of drugs known as cholinesterase inhibitors (ChEIs) which increase the activity of the neurotransmitter acetylcholine in the brain. Among the widely-used ChEIs, Exelon is the only treatment that inhibits both enzymes involved in the breakdown of this neurotransmitter – acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE). This may offer additional benefits over treatments which inhibit AChE alone. Exelon can maintain both memory and thinking, help with behavioural problems, and affect how patients cope with the activities of daily living. It may help them communicate better, interact socially, and participate in hobbies and activities of daily living<sup>3,4</sup>.

### **About Alzheimer's disease**

Alzheimer's disease is a progressive, degenerative disease that alters the brain, causing impaired memory, thinking and behaviour. Affecting approximately 15 million people worldwide and two to six percent of those over 65 years of age, it is the most common form of dementia and the third leading cause of death in this age group behind cardiovascular disease and cancer<sup>5</sup>. The worldwide direct costs for dementia in 2003 are estimated at \$156 billion<sup>5</sup>.

This release contains certain forward-looking statements relating to the Novartis Group's business, which can be identified by the use of forward-looking terminology such as "may", "will", "could", "if approved", "planned by", or similar expressions, or by express or implied discussions regarding potential future regulatory submissions for Exelon or the Exelon Patch, or regarding potential future revenue from Exelon or the Exelon Patch. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Exelon or the Exelon Patch to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that any regulatory submissions regarding the Exelon Patch will be made as planned or, if made, will be successful. Neither can there be any guarantee regarding potential future revenue from Exelon or the Exelon Patch. In particular, management's expectations regarding commercialization of Exelon or the Exelon Patch could be affected by, among other things, additional analysis of Exelon clinical data; new clinical data; unexpected clinical trial results; unexpected regulatory actions or delays in government regulation generally; the ability of Novartis to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing pressures; as well as factors discussed in Novartis AG's Form 20-F filed with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

### **About Novartis**

Novartis has been a leader in the neuroscience area for more than 50 years, having pioneered early breakthrough treatments for Alzheimer's disease, Parkinson's disease, attention deficit/hyperactivity disorder, epilepsy, schizophrenia and migraine. Novartis continues to be active in the research and development of new compounds, and is committed to addressing unmet medical needs and to supporting patients and their families affected by these disorders.

Novartis AG (NYSE: NVS) is a world leader in offering medicines to protect health, treat disease and improve well-being. Our goal is to discover, develop and successfully market innovative products to treat patients, ease suffering and enhance the quality of life. Novartis is the only company with leadership positions in both patented and generic pharmaceuticals. We are strengthening our medicine-based portfolio, which is focused on strategic growth platforms in innovation-driven pharmaceuticals, high-quality and low-cost generics, human vaccines and leading self-medication OTC brands. In 2005, the Group's businesses achieved net sales of USD 32.2 billion and net income of USD 6.1 billion. Approximately USD 4.8 billion was invested in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 96,000 people and operate in over 140 countries around the world. For more information, please visit <http://www.novartis.com>.

## References

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