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Press release

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# **NEW DATA SHOW AZILECT® (RASAGILINE TABLETS) PROVIDED CLINICAL BENEFIT IN PATIENTS WITH EARLY PARKINSON'S WHEN ADDED TO SUBOPTIMALLY CONTROLLED PATIENTS ON DOPAMINE AGONIST THERAPY**

**Results add to evidence for Azilect as an effective and well-tolerated treatment option at different stages of the progression of Parkinson's disease (PD).**

H. Lundbeck A/S (Lundbeck) and Teva Pharmaceutical Industries Ltd. (Teva) announced today that a study double-blind, placebo controlled, randomized, multicenter of Azilect® (rasagiline tablets) met its primary endpoint. The study, known as ANDANTE (Add on to Dopamine AgoNists in the TrEatment of Parkinson's disease), assessed the efficacy and tolerability of Azilect as add-on treatment to dopamine agonists compared to placebo. While the efficacy of Azilect as adjunct to levodopa has been established in previous studies (leading to its indication as adjunct therapy to levodopa) its efficacy in combination with dopamine agonist monotherapy has not previously been studied..

Results from the study demonstrated that the addition of Azilect 1mg/day provided a statistically significant improvement [Primary endpoint: treatment effect  $\pm$  SE  $-2.4 \pm 0.95$  (95% CI  $-4.3, -0.5$ ,  $p=0.012$ )] in total Unified Parkinson's Disease Rating Scale (UPDRS) score (Parts I, II and III, version three) from baseline to week 18 in patients sub-optimally controlled with dopamine agonist monotherapy compared to placebo. Azilect was well-tolerated with no significant difference in adverse events compared to placebo.

"The positive outcome of this study is important news for the PD community, for patients and physicians," said Robert A. Hauser, M.D., M.B.A., Director, Parkinson's Disease & Movement Disorders Center at the University of South Florida and primary investigator of the study. "In addition to rasagiline providing symptomatic benefit to patients sub-optimally controlled with dopamine agonist monotherapy, the study confirmed that rasagiline is well-tolerated and provided proof-of-concept for adding rasagiline to dopamine agonist therapy."

As a monoamine oxidase B (MAO-B) inhibitor, Azilect acts by increasing available synaptic dopamine. This mode of action provided the rationale for add-on therapy to dopamine agonists in the management of PD.

"The ANDANTE data continue to clarify the clinical profile of Azilect and the role it plays in helping to meet the needs of those living with PD, at multiple points in the progression of their disease," said Michael Hayden, President of Global R&D and Chief Scientific Officer at

Teva. "Teva is committed to the continued research and understanding of Azilect in PD and to sharing important findings like these with the scientific community."

"We are pleased with the results of the study as they reinforce the efficacy and tolerability profile we've seen in the clinical development programme for Azilect," said Anders Gersel Pedersen, Executive Vice President, Research and Development, at Lundbeck. "ANDANTE exemplifies Lundbeck's long-term commitment to championing treatment advances that meet the specific needs of the CNS communities we serve, including patients, healthcare providers, care partners and advocates."

The results of the study will be presented today as part of the Emerging Science program (formerly known as Late-Breaker Science) at the 65th American Academy of Neurology (AAN) Annual Meeting in San Diego, California on Wednesday, March 20, 2013. Full data from the study will be submitted for publication.

### **Study details**

ANDANTE was an 18-week, double-blind, placebo controlled, randomized, multi-center study assessing the safety and clinical benefit of rasagiline compared to placebo as add on therapy to stable dose of dopamine agonists (DAs) in the treatment of early PD.

In addition to the above stated primary endpoint results data from the secondary endpoint analysis showed the addition of Azilect® resulted in a statistically significant improvement in the UPDRS motor examination subscale (Part III) ( $p=0.007$ ). There were no significant differences between groups for the activities of daily living (ADL) ( $p=0.301$ ) or CGI-I scores. Azilect was well-tolerated in the study.

ANDANTE was conducted at 50 research sites in the United States. A total of 328 patients on sub-optimal DA monotherapy randomized into the study to add-on treatment with Azilect (N=163) or placebo (N=165). Volunteers returned to the clinic at nine weeks for an interim visit and again at 18 weeks, for an end of study visit.

To be enrolled patients needed to be on a stable DA monotherapy for  $\geq 30$  days. Patients included could not receive an optimal therapeutic dose of DAs due to intolerable side effects or were no longer experiencing sufficient control of their PD symptoms and required an additional therapeutic agent. Rescue treatment with levodopa was allowed once the patient had started treatment with study drug and had completed four weeks of treatment. DA therapy could not be adjusted during the study.

The side effect profile of Azilect as add on to DA therapy was evaluated for changes in nature and frequency of dopaminergic adverse events.

### **About Azilect®**

Azilect® is indicated for the treatment of idiopathic Parkinson's disease (PD) as monotherapy (without levodopa) or as adjunct therapy (with levodopa) in patients with end of dose fluctuations.

Azilect® is currently available in more than 40 countries worldwide, including the U.S., Canada, Israel, Mexico, and all EU countries. Teva has a long-term agreement for the joint development and marketing of Azilect® in Europe and some additional markets with H. Lundbeck A/S. In North America, Azilect® is marketed by Teva's wholly-owned subsidiary, Teva Neuroscience, Inc. ([www.tevaneuro.com](http://www.tevaneuro.com)).

**Azilect® ABBREVIATED PRESCRIBING INFORMATION (RASAGILINE)**

*Presentation: Tablets containing 1 mg of Rasagiline. Therapeutic Indications: AZILECT is indicated for the treatment of idiopathic Parkinson's disease (PD) as monotherapy (without levodopa) or as adjunct therapy (with levodopa) in patients with end of dose fluctuations. Posology and Method of Administration: Rasagiline is administered orally, at a dose of 1 mg once daily with or without levodopa. It may be taken with or without food. Elderly: No change in dose is required for elderly patients. Patients with hepatic impairment: Rasagiline use in patients with severe hepatic impairment is contraindicated. Rasagiline use in patients with moderate hepatic impairment should be avoided. Caution should be used when initiating treatment with rasagiline in patients with mild hepatic impairment. In case patients progress from mild to moderate hepatic impairment rasagiline should be stopped. Contraindications: Hypersensitivity to the active substance or to any of the excipients. Concomitant treatment with other monoamine oxidase (MAO) inhibitors (including medicinal and natural products without prescription e.g. St. John's Wort) or pethidine. At least 14 days must elapse between discontinuation of rasagiline and initiation of treatment with MAO inhibitors or pethidine. Rasagiline is contraindicated in patients with severe hepatic impairment. Special Warnings and Precautions: The concomitant use of rasagiline and fluoxetine or fluvoxamine should be avoided. At least five weeks should elapse between discontinuation of fluoxetine and initiation of treatment with rasagiline. At least 14 days should elapse between discontinuation of rasagiline and initiation of treatment with fluoxetine or fluvoxamine. The concomitant use of rasagiline and dextromethorphan or sympathomimetics such as those present in nasal and oral decongestants or cold medicinal product containing ephedrine or pseudoephedrine is not recommended. During the clinical development program, the occurrence of cases of melanoma prompted the consideration of a possible association with rasagiline. The data collected suggests that Parkinson's disease, and not any medicinal products in particular, is associated with a higher risk of skin cancer (not exclusively melanoma). Any suspicious skin lesion should be evaluated by a specialist. Caution should be used when initiating treatment with rasagiline in patients with mild hepatic impairment. Rasagiline use in patients with moderate hepatic impairment should be avoided. In case patients progress from mild to moderate hepatic impairment, rasagiline should be stopped. Interactions: Rasagiline must not be administered along with other MAO inhibitors (including medicinal and natural products without prescription e.g. St. John's Wort) as there may be a risk of non-selective MAO inhibition that may lead to hypertensive crisis. Serious adverse reactions have been reported with the concomitant use of pethidine and MAO inhibitors including another selective MAO-B inhibitor. The concomitant administration of rasagiline and pethidine is contraindicated. With MAO inhibitors there have been reports of medicinal product interactions with the concomitant use of sympathomimetic medicinal products. Therefore, in view of the MAO inhibitory activity of rasagiline, concomitant administration of rasagiline and sympathomimetics such as those present in nasal and oral decongestants or cold medicinal products, containing ephedrine or pseudoephedrine. Concomitant administration of rasagiline and dextromethorphan is not*

*recommended. The concomitant use of rasagiline and fluoxetine or fluvoxamine should be avoided. Serious adverse reactions have been reported with the concomitant use of SSRIs, SNRIs, tricyclic/ tetracyclic antidepressants and MAO inhibitors in clinical trials. Therefore, in view of the MAO inhibitory activity of rasagiline, antidepressants should be administered with caution. Fertility, Pregnancy and Lactation: No clinical data on exposed pregnancies is available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women. Undesirable Effects: Monotherapy: In parentheses is the adverse reaction incidence (% of patients) in rasagiline vs. placebo, respectively. Adverse reactions with at least 2% difference over placebo are: Influenza (4.7% vs. 0.7%), depression (5.4% vs. 2%), headache (14.1% vs. 11.9%), conjunctivitis (2.7% vs. 0.7%), rhinitis (3.4% vs. 0.7%), dermatitis (2.0% vs. 0%), musculoskeletal pain (6.7% vs. 2.6%), neck pain (2.7% vs. 0%), malaise (2% vs. 0%). Adjunct Therapy: In parentheses is the adverse reaction incidence (% of patients) in rasagiline vs. placebo, respectively. Adverse reactions with at least 2% difference over placebo are: Dyskinesia (10.5% vs. 6.2%), orthostatic hypotension (3.9% vs. 0.8%), abdominal pain (4.2% vs. 1.3%), constipation (4.2% vs. 2.1%), nausea and vomiting (8.4% vs. 6.2%), decreased weight (4.5% vs. 1.5%). Overdose: There is no specific antidote. In case of overdose, patients should be monitored and the appropriate symptomatic and supportive therapy instituted. Marketing Authorisation Holder: Teva Pharma GmbH, Graf-Arco Str. 3, 89079 Ulm, Germany.*

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#### **About Lundbeck**

Lundbeck is a global pharmaceutical company highly committed to improving the quality of life of people living with brain diseases. For this purpose, Lundbeck is engaged in the entire value chain throughout research, development, production, marketing and sales of pharmaceuticals across the world. The company's products are targeted at disorders such as depression and anxiety, psychotic disorders, epilepsy, Huntington's, Alzheimer's and Parkinson's diseases. Lundbeck's pipeline consists of several mid- to late- stage development programs.

Lundbeck employs more than 5,800 people worldwide, 2,000 of whom are based in Denmark. We have employees in 57 countries, and our products are registered in more than 100 countries. We have research centres in Denmark, China and the United States and



production facilities in Italy, France, Mexico, China and Denmark. Lundbeck generated revenue of approximately DKK 15 billion in 2012. For additional information, we encourage you to visit our corporate site [www.lundbeck.com](http://www.lundbeck.com).

### **About Teva**

Teva Pharmaceutical Industries Ltd. (NYSE: TEVA) is a leading global pharmaceutical company, committed to increasing access to high-quality healthcare by developing, producing and marketing affordable generic drugs as well as innovative and specialty pharmaceuticals and active pharmaceutical ingredients. Headquartered in Israel, Teva is the world's leading generic drug maker, with a global product portfolio of more than 1,000 molecules and a direct presence in about 60 countries. Teva's branded businesses focus on CNS, oncology, pain, respiratory and women's health therapeutic areas as well as biologics. Teva currently employs approximately 46,000 people around the world and reached \$20.3 billion in net revenues in 2012.

### **Teva's Safe Harbor Statement under the U. S. Private Securities Litigation Reform Act of 1995:**

*This release contains forward-looking statements, which express the current beliefs and expectations of management. Such statements are based on management's current beliefs and expectations and involve a number of known and unknown risks and uncertainties that could cause our future results, performance or achievements to differ significantly from the results, performance or achievements expressed or implied by such forward-looking statements. Important factors that could cause or contribute to such differences include risks relating to: our ability to develop and commercialize additional pharmaceutical products, competition for our innovative products, especially Copaxone® (including competition from innovative orally-administered alternatives, as well as from potential purported generic equivalents), competition for our generic products (including from other pharmaceutical companies and as a result of increased governmental pricing pressures), competition for our specialty pharmaceutical businesses, our ability to achieve expected results through our innovative R&D efforts, the effectiveness of our patents and other protections for innovative products, decreasing opportunities to obtain U.S. market exclusivity for significant new generic products, our ability to identify, consummate and successfully integrate acquisitions, the effects of increased leverage as a result of recent acquisitions, the extent to which any manufacturing or quality control problems damage our reputation for high quality production and require costly remediation, our potential exposure to product liability claims to the extent not covered by insurance, increased government scrutiny in both the U.S. and Europe of our agreements with brand companies, potential liability for sales of generic products prior to a final resolution of outstanding patent litigation, including that relating to the generic version of Protonix®, our exposure to currency fluctuations and restrictions as well as credit risks, the effects of reforms in healthcare regulation and pharmaceutical pricing and reimbursement, any failures to comply with complex Medicare and Medicaid reporting and payment obligations, governmental investigations into sales and marketing practices (particularly for our specialty pharmaceutical products), uncertainties surrounding the legislative and regulatory pathway for the registration and approval of biotechnology-based products, adverse effects of political or economical instability, corruption, major hostilities or acts of terrorism on our significant worldwide operations, interruptions in our supply chain or*



*problems with our information technology systems that adversely affect our complex manufacturing processes, any failure to retain key personnel or to attract additional executive and managerial talent, the impact of continuing consolidation of our distributors and customers, variations in patent laws that may adversely affect our ability to manufacture our products in the most efficient manner, potentially significant impairments of intangible assets and goodwill, potential increases in tax liabilities, the termination or expiration of governmental programs or tax benefits, environmental risks and other factors that are discussed in our Annual Report on Form 20-F for the year ended December 31, 2012 and in our other filings with the U.S. Securities and Exchange Commission. Forward-looking statements speak only as of the date on which they are made and the Company undertakes no obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.*