

# Newly Published Phase III Exploratory Analysis Suggests Investigational Oral Laquinimod for Multiple Sclerosis May Reduce Brain Damage Caused by Neurodegeneration

- Pre-planned analysis of over 1,000 patients published online in the Journal of Neurology,
   Neurosurgery & Psychiatry demonstrates the benefits of laquinimod on neurodegeneration
- Laquinimod-treated patients accumulated significantly less brain tissue damage caused by neurodegeneration, compared to placebo in MRI analyses
- Teva planning clinical trial in primary progressive multiple sclerosis (PPMS) based on novel MOA demonstrated in Phase III trial program

Jerusalem & Lund, Sweden, October 1, 2013 – Teva Pharmaceutical Industries Ltd. (NYSE: TEVA) and Active Biotech (NASDAQ OMX NORDIC: ACTI) announced today the publication of a pre-planned analysis of the Phase III ALLEGRO study demonstrating that once-daily oral laquinimod provides a beneficial impact on brain tissue damage, one of the most destructive aspects of multiple sclerosis. These data, "Placebo-controlled trial of oral laquinimod in multiple sclerosis: MRI evidence of an effect on brain tissue damage," published online in September by the Journal of Neurology, Neurosurgery & Psychiatry (JNNP), along with an accompanying editorial titled, "Oral laquinimod for multiple sclerosis: beyond the anti-inflammatory effect," can be found on the JNNP website at <a href="https://www.innp.bmj.com">www.innp.bmj.com</a>.

"This Phase III sub-study was pre-planned to explore the ability of laquinimod to act on mechanisms leading to irreversible brain tissue damage," said Professor Massimo Filippi, Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University. "This study indicates that laquinimod likely exerts a favorable effect on several MRI metrics of neurodegeneration, which in turn might explain the previously observed ability of the drug to significantly slow down progression of locomotor disability in relapsing-remitting multiple sclerosis."

The results showed that when compared with placebo, patients treated with laquinimod experienced decreased rates in brain tissue damage shown by various MRI markers. Specifically, patients receiving laquinimod showed decreased rates of white matter (WM), grey matter (GM) and thalamic atrophy; developed fewer permanent black holes (PBH); and accumulated less damage in normal appearing brain tissue (NABT), WM and GM, when compared to patients receiving placebo.

"These analyses reinforce our faith in the potential of laquinimod and we are proud to announce that we plan to initiate a clinical trial of the drug in PPMS to gather even more evidence of this novel mechanism of action," said Dr. Michael Hayden, President of Global R&D and Chief Scientific Officer for Teva Pharmaceutical Industries Ltd. "We also believe the potential neuroprotective benefits of laquinimod could have significant application in the treatment of other diseases like Crohn's disease, lupus nephritis, Huntington's disease and Alzheimer's."

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A third Phase III laquinimod trial, CONCERTO, is evaluating two doses of the investigational product (0.6mg and 1.2mg) in approximately 1,800 patients for up to 24 months. The primary outcome measure is the time to confirmed disability progression as measured by the EDSS. The study will also examine the impact of laquinimod on endpoints such as percent change in brain volume, as well as other clinical and MRI markers of disease activity.

## **ABOUT THE ALLEGRO STUDY**

ALLEGRO was a two-year multi-national, multi-center randomized, double blind, placebo-controlled study designed to evaluate the efficacy, safety and tolerability of laquinimod in MS patients. The study was conducted at 139 sites in 24 countries and enrolled 1,106 MS patients. Patients were randomized to receive a once-daily oral dose of 0.6 mg laquinimod or matching placebo. The primary outcome measure was the number of confirmed relapses; secondary measures included confirmed disability progression and changes in MRI active lesions.

In the ALLEGRO study, laquinimod showed a statistically significant 23 percent reduction in annualized relapse rate (p=0.0024), the primary endpoint, along with a significant 36 percent reduction in the risk of confirmed disability progression, as measured by Expanded Disability Status Scale (EDSS) (p=0.0122). Treatment with laquinimod was also associated with a significant reduction in brain tissue loss, as measured by a 32.8 percent reduction in progression of brain atrophy (p<0.0001).

In these MRI analyses, white matter (WM), grey matter (GM) and thalamic fractions were derived at baseline, and months 12 and 24. Also assessed were evolution of gadolinium enhancing and/or new T2 lesions into permanent black holes (PBH); magnetization transfer ratio (MTR) of normal-appearing brain tissue (NABT), WM, GM and T2 lesions as assessed by magnetization transfer (MT) MRI; and changes in n-acetylaspartate/creatinine (NAA/Cr) levels.

Eighty percent of laquinimod and 77 percent of placebo patients completed the two-year study. Patients who completed the ALLEGRO study were offered to join an open-label extension phase, in which they are being treated with laquinimod 0.6 mg daily.

The safety and tolerability profile of laquinimod observed in the ALLEGRO and BRAVO studies was favorable. The overall frequencies of adverse events, including incidence of infections, were similar to those observed in the placebo group. The most commonly reported adverse events were headaches, nasopharyngitis and back pain. The incidence of liver enzyme elevation was higher in laquinimod treated patients; however, these elevations were transient, asymptomatic and reversible.

# **ABOUT LAQUINIMOD**

Laquinimod is an oral, investigational, CNS-active immunomodulator with a novel mechanism of action being developed for the treatment of relapsing-remitting MS (RRMS). The global Phase III clinical development program evaluating oral laquinimod in MS includes two pivotal studies, ALLEGRO and BRAVO. A third Phase III laquinimod trial, CONCERTO, is evaluating two doses of

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the investigational product (0.6mg and 1.2mg) in approximately 1,800 patients for up to 24 months. The primary outcome measure is the time to confirmed disability progression as measured by the EDSS.

In addition to the MS clinical studies, laquinimod is currently in Phase II of development for Crohn's disease and lupus nephritis. Because of the neuroprotective findings, Teva is evaluating further studies to determine the effectiveness of laquinimod in treating patients with primary progressive multiple sclerosis, Huntington's disease and Alzheimer's disease.

#### **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.

## **ABOUT ACTIVE BIOTECH**

Active Biotech AB (NASDAQ OMX NORDIC: ACTI) is a biotechnology company with focus on autoimmune/inflammatory diseases and cancer. Projects in pivotal phase are laquinimod, an orally administered small molecule with unique immunomodulatory properties for the treatment of multiple sclerosis, tasquinimod for prostate cancer and ANYARA primarily for the treatment of renal cell cancer. In addition, laquinimod is also in Phase II development for Crohn's and Lupus. The company also has one additional project in clinical development, the orally administered compound paquinimod (57-57) for systemic sclerosis. Please visit <a href="http://www.activebiotech.com">http://www.activebiotech.com</a> for more information.

#### 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, 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

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and payment obligations, governmental investigations into sales and marketing practices (particularly for our specialty pharmaceutical products), uncertainties surrounding the legislative and regulatory pathways 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 fillings 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.

#### Active Biotech's Safe Harbor Statement in Accordance with the Swedish Securities Market Act:

This press release contains certain forward-looking statements. Such forward-looking statements involve known and unknown risks, uncertainties and other important factors that could cause the actual results, performance or achievements of the company, or industry results, to differ materially from any future results, performance or achievement implied by the forward-looking statements. The company does not undertake any obligation to update or publicly release any revisions to forward-looking statements to reflect events, circumstances or changes in expectations after the date of this press release.

Active Biotech is obligated to publish the information contained in this press release in accordance with the Swedish Securities Market Act. This information was provided to the media for publication 2:00 pm CET on October 1, 2013.

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