Biogen Reports Top-Line Results from Phase 3 Study Evaluating Natalizumab in Secondary Progressive MS

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ASCEND Phase 3 Trial Did Not Meet Primary and Secondary Endpoints; Natalizumab Demonstrated Statistically Significant Effect on Upper Limb Function in Patients

CAMBRIDGE, Mass.--(BUSINESS WIRE)--The Phase 3 ASCEND study investigating natalizumab in the treatment of secondary progressive multiple sclerosis (SPMS) did not achieve its primary and secondary endpoints, Biogen (NASDAQ: BIIB) reported today. During the study, natalizumab was generally well tolerated and adverse events were consistent with its known safety profile.

ASCEND evaluated the efficacy and safety of natalizumab to slow the accumulation of disability progression unrelated to relapse in SPMS patients, an unmet medical need. The majority of study participants had EDSS scores of 6.0 to 6.5 (walking aid required) and were non-relapsing for two years prior to enrollment in the study. The study's composite primary endpoint evaluated the percentage of patients whose disability had progressed on one or more of three disability measurements comprising the composite endpoint.

Natalizumab demonstrated a statistically significant effect on upper limb function (one of the three components of the primary composite endpoint) unrelated to relapses. Consistent with the established effects of natalizumab in relapsing multiple sclerosis, analyses of exploratory endpoints suggest that some patients received a benefit from treatment, including reduction of relapses and new MRI lesions.

"While we're disappointed with these results, we believe this research will provide the MS community important insights into this more advanced patient population, and the benefits that natalizumab may provide in areas such as upper limb function," said Alfred Sandrock, M.D., Ph.D., group senior vice president and chief medical officer at Biogen. "Given the challenges of treating this advanced stage of MS, these results underscore the importance of treatment early in the course of disease with effective disease-modifying therapies before a patient advances to SPMS."

SPMS is characterized by ongoing nerve damage or loss and patients experience disability progression with increasingly less frequent relapses. Despite extensive clinical research, treatment options for patients with SPMS are extremely limited and none have demonstrated efficacy in slowing the progression of disability unrelated to relapse.

Natalizumab is a high-efficacy treatment for patients with relapsing forms of MS, including relapsing-remitting MS. The safety and efficacy of natalizumab has been established across a robust clinical program and real-world use with more than a decade of clinical experience demonstrating its benefits on disease progression and sustained efficacy in relapsing MS with a well-characterized safety profile.

Detailed results from ASCEND will be presented at a future medical conference.

About ASCEND

ASCEND (A Study to Characterize the Efficacy of Natalizumab on Disability in SPMS) was a randomized, double-blind, placebo-controlled, Phase 3 trial involving 889 patients in 15 countries. Participants were randomized to receive either natalizumab 300 mg or placebo intravenously every four weeks for 96 weeks.

The primary endpoint of the study was the percentage of patients with confirmed progression of disability on one or more components of ASCEND's composite endpoint**:** the Expanded Disability Status Scale (EDSS), Timed 25-Foot Walk (T25FW) and the 9-Hole Peg Test (9HPT) where progression was confirmed at a second visit at least 6 months later and at week 96.

About TYSABRI® (natalizumab)

TYSABRI is a DMT approved in more than 65 countries. In the United States, TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of MS. In the European Union, it is indicated as a single DMT in highly active relapsing-remitting MS for adult patients who have high disease activity despite treatment with a beta interferon or glatiramer acetate or patients with rapidly evolving severe RRMS.

TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain which usually leads to death or severe disability. Risk factors that increase the risk of PML are presence of anti-JCV antibodies, prior immunosuppressant use, and longer TYSABRI treatment duration. Patients who have all three risk factors have the highest risk of developing PML. TYSABRI increases the risk of developing encephalitis and meningitis caused by herpes simplex and varicella zoster viruses. Serious, life-threatening, and sometimes fatal cases have been reported in the postmarketing setting in multiple sclerosis patients receiving TYSABRI. Clinically significant liver injury has also been reported in the post-marketing setting.

Other serious adverse events that have occurred in TYSABRI-treated patients include hypersensitivity reactions (e.g., anaphylaxis) and infections, including opportunistic and other atypical infections.

TYSABRI has advanced the treatment of MS patients with its proven ability to slow the progression of disability, reduce relapse rates, and impact the number of MRI brain lesions with a well-characterized safety profile. Data from the Phase 3 AFFIRM trial, which was published in the *New England Journal of Medicine*, showed that at two years, TYSABRI treatment led to a 67 percent relative reduction ($p<0.001$) in the annualized relapse rate when compared with placebo and reduced the relative risk of disability progression by 42 percent ($p<0.001$).

TYSABRI is a monoclonal antibody that selectively binds to α4-integrin and is thought to interrupt the activity of inflammatory cells in MS patients by blocking the interaction between α4β1-integrin and vascular cell adhesion molecule-1. Disruption of these molecular interactions prevents transmigration of leukocytes across the endothelium into inflamed parenchymal tissue. The specific mechanism(s) by which TYSABRI exerts its effects in multiple sclerosis have not been fully defined.

For additional important safety information, and the United States full prescribing information, please visit www.TYSABRI.com or your respective country's website.

About Biogen

Through cutting-edge science and medicine, Biogen discovers, develops and delivers to patients worldwide innovative therapies for the treatment of neurodegenerative diseases, hematologic conditions and autoimmune disorders. Founded in 1978, Biogen is one of the world's oldest independent biotechnology companies and patients worldwide benefit from its leading multiple sclerosis and innovative hemophilia therapies. For product labeling, press releases and additional information about the company, please visit www.biogen.com.

Safe Harbor

This press release contains forward-looking statements, including statements about potential insights into treatments for SPMS. These statements may be identified by words such as "believe," "expect," "may," "plan," "potential," "will" and similar expressions, and are based on the company's current beliefs and expectations. Drug development involves a high degree of risk, and only a small number of research and development programs results in the commercialization of a product or additional product indications. Success in preclinical work or early stage clinical trials does not ensure that later stage or larger scale clinical trials will be successful. For more detailed information on the risks and uncertainties associated with Biogen's drug development activities, please review the Risk Factors section of Biogen's most recent annual or quarterly report filed with the Securities and Exchange Commission. Any forward-looking statements speak only as of the date of this press release and the company assumes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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