New Analysis of Risk Stratification for TYSABRI® Published in New England Journal of Medicine

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- Use of Biomarker has Potential to Advance Personalized Treatment for MS Patients -

WESTON, Mass. & DUBLIN--(BUSINESS WIRE)--Biogen Idec (NASDAQ: BIIB) and Elan Corporation, plc (NYSE: ELN) today announced that the *New England Journal of Medicine* published research from the companies' global risk management program that updates the risk of TYSABRI ® (natalizumab)-associated progressive multifocal leukoencephalopathy (PML), an infrequent but serious brain infection that usually leads to death or severe disability, in people with multiple sclerosis (MS). The analysis looked at three risk factors associated with a patient's PML risk: anti-JC virus (JCV) antibody status, use of immunosuppressant (IS) therapy prior to TYSABRI initiation, and longer duration of treatment with TYSABRI.

Biogen Idec and Elan developed the quantitative risk stratification algorithm to help physicians and people with MS have more confidence in their treatment decisions when considering TYSABRI, a highly effective treatment for relapsing forms of MS.

"By identifying these risk factors and incorporating them into our risk stratification algorithm, we bring the advantages of personalized medicine to MS," said Alfred Sandrock, M.D., Ph.D., senior vice president, development science and chief medical officer, Biogen Idec. "This approach to treatment is intended to help patients better understand their individual benefit-risk profiles when considering TYSABRI as a treatment option."

About the Research
Researchers used data from clinical studies, post-marketing sources, and an independent Swedish registry to estimate the incidence of PML among TYSABRI-treated patients. Data as of Feb 29, 2012 from 212 confirmed cases of PML among 99,571 TYSABRI-treated patients were used to develop a risk stratification algorithm based on three established risk factors for PML: anti-JCV antibody status, prior use of IS therapy, and duration of treatment with TYSABRI (one to 24 months vs. 25 to 48 months). Based on the presence or absence of these risk factors, patients were divided into distinct subgroups at lower or higher risk for the development of PML.

Blood samples from 5,896 MS patients who participated in three clinical studies - AFFIRM , STRATIFY-1, and the U.S. arm of the TYSABRI Global Observational Program in Safety [TYGRIS] study - as well as blood samples from patients included in the Swedish Multiple Sclerosis registry, were tested for anti-JCV antibodies.

In addition, data from 54 TYSABRI-treated patients who developed PML and had blood samples collected six to 187 months before they were diagnosed with PML were tested for anti-JCV antibodies; all samples tested positive for anti-JCV antibodies.

Data on prior IS use were not available for all patients taking TYSABRI. Therefore, the proportion of prior IS use within the global TYGRIS studies (U.S. and Rest of World) were used to estimate prior IS use in the overall TYSABRI-treated population.

Results
The risk of PML increased with longer duration of TYSABRI treatment, with the greatest increase observed after two years of therapy. Data beyond four years of therapy were limited.

Prior IS use was more common in patients who developed PML (34.5%) compared to patients in the global TYGRIS study (20.3%), indicating that prior IS use was associated with an increased risk of PML.

The prevalence of anti-JCV antibodies in the general MS population was 54.9 percent (95% confidence interval [CI], 53.7 – 56.2) and differed from the 100 percent anti-JCV antibody positivity observed in the 54 MS patients who developed PML and had known pre-PML anti-JCV antibody status. Because all 54 MS patients with known pre-PML anti-JCV antibody status tested positive, a sensitivity analysis assuming one hypothetical anti-JCV antibody negative PML patient was used to estimate the PML risk in antibody negative patients.

Anti-JCV antibody status, combined with prior IS use and TYSABRI treatment duration were used to stratify patients at lower or higher risk for the development of PML. There was an approximately 120-fold difference between patients in the lowest and highest risk groups. Patients who were anti-JCV antibody negative were at the lowest risk for PML with an estimated risk of 0.09 cases or fewer per 1,000 patients (95% CI, 0 to 0.48).

The highest risk of PML was found in patients who had received 25 to 48 months of TYSABRI treatment, had been treated with an IS therapy before TYSABRI treatment was initiated, and were positive for anti-JCV antibodies. The PML incidence in this group was estimated to be 11.1 cases per 1,000 patients (95% CI, 8.3 to 14.5).

The authors concluded that data from prospective studies are needed to further characterize these risks.

"Although TYSABRI has proven efficacy, the risk of PML has been a cause of concern for patients," said Ted Yednock, head of global research at Elan. "This analysis illustrates how the risk stratification model we have developed with Biogen Idec can help physicians and MS patients make more informed treatment decisions."

About the Risk Stratification
The TYSABRI U.S. label and EU Summary of Product Characteristics were updated to add anti-JCV antibody status as a risk factor for PML. In addition to prior IS therapy and duration of TYSABRI therapy, anti-JCV antibody status is the third factor in the risk stratification model developed by Biogen Idec and Elan that helps identify a patient's risk for developing PML. Physicians can determine their MS patient's anti-JCV antibody status by using the STRATIFY JCV assay, the first blood test to be market authorized for the qualitative detection of antibodies to the polyomavirus JC virus.

At the time of this analysis (February 29, 2012), more than 99,500 patients had been treated with TYSABRI and there were 212 confirmed cases of PML (2.1 cases per 1, 000 patients).

About TYSABRI
TYSABRI is approved in more than 65 countries. TYSABRI is approved in the United States as a monotherapy for relapsing forms of MS, generally for patients who have had an inadequate response to, or are unable to tolerate, an alternative MS therapy. In the European Union, it is approved for highly active relapsing-remitting MS (RRMS) in adult patients who have failed to respond to beta interferon or have rapidly evolving, severe RRMS.

TYSABRI has advanced the treatment of MS patients with its established efficacy. Data from the Phase 3 AFFIRM trial, which was published in the New England Journal of Medicine, showed that after two years, TYSABRI treatment led to a 68 percent relative reduction ($p<0.001$) in the annualized relapse rate when compared with placebo and reduced the relative risk of disability progression by 42-54 percent ($p<0.001$).

TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain, which usually leads to death or severe disability. Infection by the JC virus (JCV) is required for the development of PML and patients who are anti-JCV antibody positive have a higher risk of developing PML. 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. 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. Clinically significant liver injury has also been reported in the post-marketing setting. A list of adverse events can be found in the full TYSABRI product labeling for each country where it is approved.

TYSABRI is marketed and distributed by Biogen Idec Inc. and Elan Corporation, plc. For full prescribing information, including boxed warning and important safety information, and more information about TYSABRI, please visit www.biogenidec.com or www.elan.com.

About Biogen Idec
Through cutting-edge science and medicine, Biogen Idec discovers, develops and delivers to patients worldwide innovative therapies for the treatment of neurodegenerative diseases, hemophilia and autoimmune disorders. Founded in 1978, Biogen Idec is the world's oldest independent biotechnology company. Patients worldwide benefit from its leading multiple sclerosis therapies, and the company generates more than $5 billion in annual revenues. For product labeling, press releases and additional information about the company, please visit www.biogenidec.com.

About Elan
Elan Corporation, plc is a neuroscience-focused biotechnology company committed to making a difference in the lives of patients and their families by dedicating itself to bringing innovations in science to fill significant unmet medical needs that continue to exist around the world. Elan shares trade on the New York and Irish Stock Exchanges. For additional information about Elan, please visit www.elan.com.

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