



## Data about Early Use and Long-Term Benefit of TYSABRI Presented at 5th Joint Triennial Congress ofECTRIMS and ACTRIMS

October 19, 2011

--Results of Research Further Supporting PML Risk Stratification Also Presented--

WESTON, Mass. & DUBLIN--([BUSINESS WIRE](#))--[Biogen Idec](#) (NASDAQ: BIIB) and [Elan Corporation, plc](#) (NYSE: ELN) today announced 28 company-supported TYSABRI® (natalizumab) presentations at the 5<sup>th</sup> Joint Triennial Congress of the European and Americas Committees for Treatment and Research in Multiple Sclerosis (ECTRIMS and ACTRIMS), held in Amsterdam, the Netherlands.

Key data indicated patients on TYSABRI experienced reduced annualized relapse rates (ARR), particularly in those treated with TYSABRI early in the course of their disease. Data also indicated a long-term benefit for patients who had achieved freedom from disease activity early in their treatment course. Data from a separate study showed TYSABRI-treated patients experienced improved incontinence-related quality of life (QOL). Additional data sets were presented further supporting Biogen Idec's and Elan's efforts to stratify the risk of progressive multifocal leukoencephalopathy (PML) in TYSABRI-treated patients.

"Continued study of patient experience with TYSABRI has shown it can potentially improve the lives of people with MS by delaying disease progression and improving incontinence-related quality of life," said Douglas E. Williams, Ph.D., Executive Vice President, Research and Development at Biogen Idec. "The efficacy data from TOP and STRATA have shown the potential benefits of TYSABRI treatment early in the course of the disease, and these benefits were maintained over time. These, coupled with our data-driven approach to risk stratification, help us confidently position TYSABRI for the treatment of many patients who previously may not have considered this important therapy."

"Further study of anti-JCV antibody status continues to support its utility for risk stratification, enabling a personalized discussion of benefit/risk for each individual patient," said Ted Yednock, Ph.D., Executive Vice President, Head of Global Research at Elan. "Our five years in-market experience, along with information resulting from our ongoing study of the efficacy and safety of TYSABRI in MS, enables physicians and patients to make decisions on therapeutic approaches for treating this debilitating disease."

### **Data supporting early use and long-term benefit of TYSABRI**

#### **Long-term outcomes in natalizumab-treated patients who were free of disease activity over the 2-year AFFIRM study – Poster 513**

This analysis compared patients in the long-term **Safety of TYSABRI Re-dosing and Treatment (STRATA)** study who were disease activity free (DAF) to patients who were not disease activity free (NDAF) over two years in the AFFIRM trial. At STRATA baseline, there were 177 DAF patients and 415 NDAF patients. Ninety four percent of the patients free of disease activity and 60 percent of the patients not free of disease activity were originally randomized to TYSABRI in AFFIRM. AFFIRM randomized patients in a 2:1 ratio (TYSABRI:placebo).

At three years of TYSABRI treatment in STRATA, the DAF patients had less disability and significantly lower ARR than the NDAF patients. Mean Expanded Disability Status Scale (EDSS) scores were 2.34 for DAF and 3.23 for NDAF patients ( $p < 0.0001$ ) and the unadjusted ARRs was 0.08 in DAF patients and 0.16 in NDAF patients ( $p < 0.0001$ ).

These data show TYSABRI-treated patients who achieve freedom from disease activity over the short term may experience longer-term benefits, as well as early treatment is preferable to delayed treatment.

This poster will be available for viewing on Thursday, 20 October between 15:30 and 17:00 CEST.

#### **Updated safety and efficacy of natalizumab in the ongoing STRATA study – Poster 981**

This study evaluated the safety and efficacy of TYSABRI in the ongoing **Safety of TYSABRI Re-dosing and Treatment Study (STRATA)** in which participants represented 3,198 patient-years of TYSABRI exposure. STRATA is an ongoing, open-label, multinational study currently in its long-term extension phase in patients who completed feeder studies and their open-label extensions.

This study showed that for patients in the overall population, ARR remained low at .17 during TYSABRI treatment, which is consistent with rates observed in the AFFIRM study and was maintained over 240 weeks. In addition ARR was lower in patients originally randomized to TYSABRI compared with patients who were originally randomized to placebo in the feeder studies: 0.15 (95% confidence interval (CI): 0.14–0.17) vs 0.22 (95% CI: 0.19–0.24). Mean EDSS scores were either stable or improved throughout STRATA and were lower in patients who originally received TYSABRI compared with those who originally received placebo in the feeder studies. The proportion of patients with sustained disability progression during STRATA remained low and stable, regardless of original treatment assignment. Overall these data suggested early treatment may be preferable to late treatment.

Further, data showed that the safety profile of TYSABRI in STRATA is consistent with the overall post-marketing safety profile of the drug.

This poster will be available for viewing on Friday, 21 October between 15:30 and 17:00 CEST.

#### **Assessment of annualized relapse rate and Expanded Disability Status Scale score changes over time in the TYSABRI (Natalizumab) Observational Program – Poster 509**

This analysis evaluated the association between baseline treatment history and ARR in the TYSABRI Observational Program (TOP). TOP assesses long-term outcomes in 3,484 TYSABRI-treated RRMS patients in five treatment-history groups: therapy naïve ( $n=337$ ); interferon (IFN) only ( $n=1626$ ); glatiramer acetate (GA) only ( $n=288$ ); switched between IFN and GA in either direction ( $n=595$ ), and prior immunosuppressant (IS) use ( $n=487$ ).

Post-baseline ARR was significantly reduced and remained low after three years of TYSABRI therapy. Mean ARRs in TYSABRI patients were lowest

in patients who were therapy naïve at baseline (0.16) and highest in patients who were previously treated with IS therapy (0.34) or who switched between GA and IFN (0.25). EDSS scores remained stable over three years in patients treated with TYSABRI. The proportion of patients with sustained improvement of EDSS scores was higher than the proportion of patients with sustained worsening (progression) of EDSS scores.

These findings indicated a potential benefit of TYSABRI treatment early in the course of the disease.

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#### TRUST study results: effects of natalizumab on bladder function – Poster 1040

In the TRUST (Evaluation of Bladder Function in Relapsing Remitting Multiple Sclerosis Patients Treated with natalizumab) study, investigators evaluated the potential effects of TYSABRI on bladder control as measured by the Urogenital Distress Inventory short form (UDI-6) score compared with baseline. The change in the Incontinence Impact Questionnaire short form (IIQ-7) was used as a secondary endpoint. At week 24, 28 patients completed the study.

Mean UDI-6 and IIQ-7 scores were both significantly lower than baseline beginning at week four and up to week 24. At week 24, 85.7 percent and 78.6 percent of patients demonstrated improvements from baseline in UDI-6 and IIQ-7 scores ( $p=0.0001$  and  $p=0.0011$ , respectively).

According to data from this open-label, single-arm, 24-week proof-of-concept study, the magnitude of the effect shows that TYSABRI may be capable of decreasing the impact of incontinence on QOL from moderate to mild. Other endpoints are currently being analyzed; final data will be presented upon study completion.

TYSABRI significantly improved incontinence-related QOL as measured by mean improvements in UDI-6 and IIQ-7 scores. Patients with worse (higher) UDI-6 or IIQ-7 scores at baseline showed greater initial improvement in scores and maintained improvement over time while receiving TYSABRI. The magnitude of this effect suggests that TYSABRI may be capable of decreasing the impact of urinary incontinence on QOL from moderate to mild. Further studies are needed to support these analyses.

This poster will be available for viewing on Friday, 21 October between 15:30 and 17:00 CEST.

#### **Additional Data Supports Risk Stratification Initiatives**

Data from two studies further support the risk stratification initiatives undertaken by Biogen Idec and Elan.

#### JCV epidemiology in MS: epidemiology of anti-JC virus antibody prevalence in multiple sclerosis patients – Poster 801

This cross-sectional, multicenter, multi-national, epidemiological study of more than 2,600 patients was designed to confirm the rate of anti-JCV antibodies in the MS patient population. This preliminary analysis showed a prevalence rate of anti-JCV antibodies of 57.0 percent in this group, which is consistent with previous studies. In addition, no significant associations were observed between anti-JCV antibody status and MS disease duration, MS type, MS therapy use, IS use, or MS treatment duration.

#### Contribution of natalizumab treatment duration, prior immunosuppressant use, and anti-JC virus antibody status to the risk of progressive multifocal leukoencephalopathy in natalizumab-treated multiple sclerosis patients – Poster 995

This analysis evaluated PML risk in MS patients based on three risk factors: TYSABRI treatment duration, prior immunosuppressant (IS) use and anti-JCV antibody serostatus. Patient blood samples and clinical data were obtained from TYSABRI post-marketing sources, clinical studies and an independent Swedish registry representing 165,500 patient-years of TYSABRI experience.

Anti-JCV antibody status, combined with prior IS and TYSABRI treatment duration can stratify patients at lower and higher risk for PML. Patients who were anti-JCV antibody negative were at lowest risk. Patients who had all three risk factors were at greatest risk.

Further, poster 981 showed the three factors had a relationship with PML since they occurred in patients who received between 33 and 58 doses of TYSABRI, were anti-JCV antibody positive, and three of the eight PML patients from the study had prior IS use. In the study, as of July 20, 2011, reported SAEs also included infections and infestations (3 percent), gastrointestinal disorders (2 percent) and neoplasms (2 percent).

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#### **About TYSABRI**

TYSABRI is approved in more than 60 countries. As a monotherapy, it is approved in the U.S. 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 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. It has been proven to reduce flare-ups and slow physical disability progression. Data from the Phase III 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 that usually leads to death or severe disability. 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 patients treated with TYSABRI in the post-marketing setting. Common adverse events reported in TYSABRI-treated MS patients include headache, fatigue, infusion reactions, urinary tract infections, joint and limb pain, and rash.

TYSABRI is co-marketed by Biogen Idec Inc. and Elan Corporation, plc. For more information about TYSABRI, please visit [www.tysabri.com](http://www.tysabri.com), [www.biogenidec.com](http://www.biogenidec.com) or [www.elan.com](http://www.elan.com), or call 1-800-456-2255.

#### **About Biogen Idec**

Biogen Idec uses cutting-edge science to discover, develop, manufacture and market therapies for serious diseases with a focus on neurology, immunology and hemophilia. 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 \$4 billion in annual revenues. For product labeling, press releases and additional information about the company, please visit [www.biogenidec.com](http://www.biogenidec.com).

## **About Elan**

Elan Corporation, plc is a neuroscience-based 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 are listed on the New York and Irish Stock Exchanges. For additional information about the company, please visit <http://www.elan.com>.

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