New Data Affirm Strong Efficacy and Well-Characterized Safety Profile of TECFIDERA® in Both Clinical Studies and Real-World Setting

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− TECFIDERA Treatment Significantly Reduced Time to First Relapse vs. Glatiramer Acetate, Interferon β and Teriflunomide and Showed Comparable Efficacy to Fingolimod in Data Analysis from MSBase Registry −

− Benefit-Risk Profile of TECFIDERA Remains Favorable Up to Nine Years −

CAMBRIDGE, Mass.--(BUSINESS WIRE)--New real-world and clinical evidence demonstrates that TECFIDERA® (dimethyl fumarate) consistently delivered strong, sustained efficacy in newly-diagnosed and previously treated patients with relapsing-remitting multiple sclerosis (RRMS) and affirms its well-characterized safety profile in patients who have had up to nine years of treatment. Biogen (NASDAQ: BIIB) will present these data at the 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in London.

“As we continue to gather both clinical and real-world data, evidence shows that TECFIDERA consistently demonstrates strong efficacy in reducing MS disease activity over the long term,” said Ralph Kern, M.D., senior vice president, Worldwide Medical, Biogen. “The findings presented at ECTRIMS confirm the results we observed in the TECFIDERA clinical trial program, further supporting its early use to improve outcomes for people living with MS.”

Comparative Real-World Data Echo Strong Efficacy of TECFIDERA Observed in Clinical Trials
Real-world evidence affirms the positive effects of TECFIDERA treatment observed in clinical trials, and demonstrates effectiveness versus multiple MS therapies.

Using data sourced from the global MSBase registry and propensity score matching, researchers compared relapse rates and discontinuation outcomes in 415 TECFIDERA-treated patients to those treated with another widely-used disease-modifying therapy (fingolimod, teriflunomide, interferon β and glatiramer acetate). MSBase is an ongoing, longitudinal, observational registry that includes data from nearly 40,000 MS patients across 72 countries.

Real-world evidence from the MSBase analysis shows significant benefits with TECFIDERA on time to first relapse relative to interferon β (26%; hazard ratio [HR] 0.74; 95% confidence interval [CI] 0.57, 0.97), glatiramer acetate (28%; HR 0.72; 95% CI 0.54, 0.95) and teriflunomide (34%; HR 0.66; 95% CI 0.45, 0.99). Time to first relapse between TECFIDERA and fingolimod was similar.

“The MSBase registry is one of the largest sources of real-world data, contributed by physicians with the ultimate goal of improving MS quality of care,” said professor Helmut Butzkueven, joint director of the Multiple Sclerosis Service at the Royal Melbourne Hospital and associate professor in the Department of Medicine, University of Melbourne. “When we conducted this comparative effectiveness research, propensity score matching helped ensure the similarity of the patient populations, which strengthened the analysis. The data showed that TECFIDERA significantly reduced the time to first relapse compared to platform therapies and teriflunomide and had comparable efficacy to fingolimod.”

The MSBase analysis also evaluated two secondary endpoints, annualized relapse rate (ARR) and treatment persistence. Longer follow-up of TECFIDERA in the real-world setting will strengthen this analysis and may clarify the effects seen on ARR across treatment groups. An increase of treatment discontinuation with TECFIDERA relative to fingolimod and interferon was also observed. A separate real-world retrospective analysis of TECFIDERA patients presented at ECTRIMS suggests that providing patient coaching can offer a potentially effective means to reduce treatment discontinuations.

Additional efficacy data presented at ECTRIMS include:

- New U.S. health claims data from a large commercial insurance database, which demonstrate the real-world effectiveness of TECFIDERA compared to other MS therapies, as supported by the MSBase registry. A new analysis of these data also shows consistent results in a subgroup of newly-diagnosed patients.
- Data from the ongoing Phase 3 ENDORSE study that show the ARR and 24-week confirmed disability progression remained low in newly-diagnosed patients treated with TECFIDERA over a minimum of seven years.

Favorable Benefit-Risk Profile Strengthened by Nine Years of Treatment Data
The safety profile of TECFIDERA remains unchanged and the overall benefit-risk remains favorable, as demonstrated by up to nine years of clinical study results and real-world evidence presented at the congress. Further, the data continue to substantiate current guidance for monitoring absolute lymphocyte counts (ALC) to effectively identify patients at risk of severe and prolonged lymphopenia.

A List of TECFIDERA ECTRIMS Data Presentations Includes:

- *Poster Session 1 – Thursday, 15 September – 15:45-17:00 PM BST*
  - Absolute Lymphocyte Count and Lymphocyte Subset Profiles During Long-Term Treatment with Delayed-Release Dimethyl Fumarate in Patients with Relapsing-Remitting Multiple Sclerosis (P716)
  - Seven-Year Follow-up of the Efficacy of Delayed-Release Dimethyl Fumarate in Newly Diagnosed Patients With Relapsing-Remitting Multiple Sclerosis: Integrated Analysis of DEFINE, CONFIRM, and ENDORSE (P631)
- *Poster Session 2 – Friday, 16 September – 15:30-17:00 PM BST*

- Comparative Analysis of Multiple Sclerosis Outcomes in Dimethyl Fumarate-Treated Patients Relative to Propensity Matched Fingolimod, Interferon, Glatiramer Acetate, or Teriflunomide (P1157)
- The Potential of Individualized Patient Coaching to Optimize Treatment With Delayed-Release Dimethyl Fumarate: A Retrospective Analysis of Patients With Multiple Sclerosis Treated in a Real-World Setting (P1214)

- *ePosters – Available in ECTRIMS Online Library and App*
  - Annual Relapse Rates in Multiple Sclerosis Patients Treated with Different Disease-Modify Therapies – Findings from a Real World Setting (EP1481)
  - Effect of Delayed-Release Dimethyl Fumarate on Lymphocyte Subsets in Patients with Relapsing Multiple Sclerosis: A Retrospective, Multicentre, Observational Study (REALIZE) (EP1495)

About ENDORSE
ENDORSE is an ongoing global, dose-blind, Phase 3 extension study to determine the long-term safety and efficacy of TECFIDERA (240 mg, BID or TID). The study has enrolled 1,738 patients with RRMS who completed the DEFINE or CONFIRM studies. Patients who received two years of TECFIDERA in DEFINE and CONFIRM continued on the same dose (BID or TID) in ENDORSE. Patients who previously received placebo or glatiramer acetate (CONFIRM only) were randomized 1:1 to TECFIDERA BID or TID. Following TECFIDERA approval at a dose of 240 mg BID, all subjects continuing in this study received open-label TECFIDERA 240 mg BID. Patients participating in ENDORSE will be followed for up to eight years.

The primary objective of the study is to evaluate the long-term safety profile of TECFIDERA. Secondary objectives include: long-term efficacy of TECFIDERA on clinical outcomes and MS brain lesions on MRI scans; and effects of TECFIDERA on quality of life measurements.

About TECFIDERA ®
TECFIDERA is an oral therapy for relapsing forms of MS, including relapsing-remitting MS, the most common form of MS. TECFIDERA is currently approved in 24 countries including the United States, the European Union, Canada, Australia and Switzerland. Through a robust clinical trial program and commercial launches starting with the United States in March 2013, more than 215,000 patients have been treated with TECFIDERA worldwide.[1]

TECFIDERA has been proven to reduce the rate of MS relapses, slow the progression of disability, and the number of MS brain lesions, while demonstrating a favorable benefit-risk profile in a broad range of patients with relapsing forms of MS. [2] In clinical trials, the most common adverse events associated with TECFIDERA were flushing and gastrointestinal (GI) events. Other side effects included a decrease in mean lymphocyte counts during the first year of treatment, which then plateaued. TECFIDERA is contraindicated in patients with a known hypersensitivity to dimethyl fumarate or any of the excipients of TECFIDERA. Rare cases of PML have been seen with TECFIDERA patients in the setting of prolonged moderate to severe lymphopenia.

The efficacy and safety of TECFIDERA have been studied in a large, global clinical program, which includes an ongoing long-term extension study. It is believed that TECFIDERA treats MS by activating the Nrf2 pathway, although its exact mechanism of action is unknown. This pathway provides a way for cells in the body to defend themselves against inflammation and oxidative stress caused by conditions like MS.

For additional important safety information, and the United States full prescribing information, please visit www.tecfidera.com.

About Biogen
Through cutting-edge science and medicine, Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological, autoimmune and rare diseases. 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 more information, please visit www.biogen.com. Follow us on Twitter.

Safe Harbor
This press release includes forward-looking statements, including statements about the benefits of TECFIDERA in MS patients over the long-term. These forward-looking statements may be accompanied by such words as "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," "will," and other words and terms of similar meaning. You should not place undue reliance on these statements. Drug development and commercialization involve a high degree of risk and only a small number of research and development programs result in commercialization of a product. Factors which could cause actual results to differ materially from our current expectations include the risk that unexpected concerns may arise from additional data or analysis, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates or expansion of our product labeling, or we may encounter other unexpected hurdles. For more detailed information on the risks and uncertainties associated with our drug development and commercialization activities, please review the Risk Factors section of our most recent annual or quarterly report filed with the Securities and Exchange Commission. These statements are based on our current beliefs and expectations and speak only as of the date of this press release. We do not undertake any obligation to publicly update any forward-looking statements.

[1] Combined post-marketing and clinical trials exposure to TECFIDERA as of 30 June 2016.
[2] TECFIDERA is approved in the European Union for relapsing-remitting multiple sclerosis.

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