TECFIDERA® (Dimethyl Fumarate) Data Reinforce Strong, Sustained Efficacy for Newly-Diagnosed MS Patients

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TECFIDERA Provides Robust and Long-Term Efficacy in Treatment-Naïve Patients and Those with Prior Interferon or Glatiramer Acetate Experience

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Biogen (NASDAQ: BIIB) today announced new data that continue to support TECFIDERA® (dimethyl fumarate) as an effective, long-term treatment for people who are living with relapsing forms of multiple sclerosis (MS). Data show TECFIDERA significantly reduced relapses and disability progression in newly-diagnosed relapsing-remitting MS (RRMS) patients who had highly active disease. Additional data indicate TECFIDERA showed strong and sustained efficacy over five years in RRMS patients who were previously treated with an interferon (interferon beta-1a/b [IFN]) or glatiramer acetate (GA). These results will be presented at the 67th American Academy of Neurology (AAN) Annual Meeting in Washington, D.C.

"Taken together, these studies reinforce that TECFIDERA delivers robust efficacy when used as a first-line therapy, as well as when it is used after a patient has discontinued interferon or glatiramer acetate treatment," said J. Theodore Phillips, M.D., Ph.D., research investigator at the Baylor Institute for Immunology Research and clinical professor of Neurology at the University of Texas Southwestern Medical Center. "In addition, strong efficacy was observed with TECFIDERA treatment in various patient populations including those with highly active MS."

Robust Efficacy in Newly-Diagnosed Patients with Highly Active MS

TECFIDERA provided robust efficacy in newly-diagnosed patients who have highly active MS, as seen in a post-hoc analysis of two years of integrated data from the Phase 3 DEFINE and CONFIRM studies. Patients included in the analysis were diagnosed with RRMS within one year prior to enrolling in the DEFINE or CONFIRM studies, were either treatment-naïve or previously treated with corticosteroids alone, and met the criteria for highly active MS (two or more relapses within one year prior to enrolling in DEFINE or CONFIRM). Compared to placebo (n=77) at two years, TECFIDERA (n=84) significantly reduced annualized relapse rate (ARR) (56% reduction, p<0.0040), the proportion of patients who relapsed (56% reduction, p=0.0037) and time to sustained 12-week progression of disability (78% reduction, p=0.0067).

"TECFIDERA continues to demonstrate consistently strong efficacy and favorable safety results that we believe support its position as the new oral standard of care," said Gilmore O'Neill, vice president, Multiple Sclerosis Research and Development at Biogen. "More than 135,000 patients have been treated with TECFIDERA worldwide since it was introduced to the market two years ago."

Long-Term Efficacy of TECFIDERA in Treatment-Naïve Patients and Those with Prior IFN/GA Treatment Experience

TECFIDERA provided consistent, long-term efficacy in patients with RRMS who were previously treated with IFN or GA, according to an integrated post-hoc analysis in a subset of patients from the Phase 3 DEFINE, CONFIRM and ENDORSE studies. Patients included in the analysis were followed for a minimum of five years (two years in DEFINE/CONFIRM plus three or more years in ENDORSE).

Throughout the study period, the ARR remained low in patients who received continuous treatment with TECFIDERA compared to those who initially received two years of placebo in DEFINE/CONFIRM. In patients who switched from placebo in DEFINE/CONFIRM to TECFIDERA in ENDORSE, improvements were observed in ARR whether they were treatment-naïve or had treated their MS with IFN or GA.

- Treatment-naïve patients:
  - Patients receiving five years of TECFIDERA (n=267): ARR was 0.123 (95% confidence interval [CI]: 0.097, 0.157)
  - Patients who switched to TECFIDERA in year three (n=133): ARR was 0.207 (95% CI: 0.152, 0.283)
- Patients treated with one or more prior IFN/GA therapy:
  - Patients receiving five years of TECFIDERA (n=124): ARR was 0.195 (95% CI: 0.151, 0.252)
  - Patients who switched to TECFIDERA in year three (n=68): ARR was 0.253 (95% CI: 0.181, 0.353)

The safety profile of TECFIDERA observed in ENDORSE in the presented analysis was consistent with the favorable findings reported in the DEFINE and CONFIRM studies, reflecting a minimum of five years of observation. There was no overall increased risk for serious infections, including opportunistic infections.

These data will be presented in poster presentations on Thursday, April 23 at 2:00 p.m. ET:

- *Long-Term Efficacy of Delayed-Release Dimethyl Fumarate for Relapsing-Remitting Multiple Sclerosis According to Prior Therapy: Integrated Analysis of the DEFINE, CONFIRM, and ENDORSE Studies* (poster P7.229)
- *Clinical Efficacy of Delayed-Release Dimethyl Fumarate in Newly Diagnosed Relapsing-Remitting Multiple Sclerosis Patients with Highly Active Disease: An Integrated Analysis of the Phase 3 DEFINE and CONFIRM Studies* (poster P7.228)

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 GA (CONFIRM only) were randomized 1:1 to TECFIDERA BID or TID. 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 DEFINE and CONFIRM

DEFINE (**D**etermination of the **E**fficacy and safety of oral **F**umarate **IN** relapsing-r**E**mitting MS) was a global, two-year, randomized, multi-center, double-blind, placebo-controlled, dose-comparison Phase 3 clinical trial that enrolled more than 1,200 patients with RRMS at 198 sites in 28 countries. The study evaluated TECFIDERA (240 mg, BID or TID) compared to placebo.

The primary objective was to determine if TECFIDERA was effective in reducing the proportion of relapsing patients at two years. Secondary endpoints included reduction in the number of new or newly enlarging T2-hyperintense lesions and Gd+ lesions as measured by MRI, reduction in ARR, and reduction of disability progression as measured by EDSS. Safety and tolerability of TECFIDERA were also assessed.

CONFIRM (**CO**mparator and a**N** oral **F**umarate **I**n **R**elapsing-remitting **M**S) was a global, two-year, randomized, multi-center, placebo-controlled, double-blind, dose-comparison Phase 3 clinical trial that enrolled more than 1,400 patients with RRMS at 200 sites in 28 countries. The study investigated TECFIDERA (240 mg, BID or TID) compared to placebo and included a reference comparator arm of glatiramer acetate (GA; 20 mg subcutaneous daily injection) versus placebo.

The primary objective was to determine whether TECFIDERA was effective in reducing the rate of clinical relapse at two years compared to the placebo group. Secondary endpoints at two years included reduction in: the number of new or newly enlarging T2-hyperintense lesions and the number of new non-enhancing T1-hypointense lesions (MRI scans were obtained at a cohort of sites); the proportion of patients who relapsed; and progression of disability as measured by EDSS. Safety and tolerability of TECFIDERA were also assessed.

About TECFIDERA®

TECFIDERA is an oral therapy for relapsing forms of MS,[1] including relapsing-remitting MS, the most common form of MS. TECFIDERA is currently approved in 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 135,000 patients have been treated with TECFIDERA worldwide.[2]

TECFIDERA has been proven to reduce rate of MS relapses, slow the progression of disability, and the number of MS brain lesions, while demonstrating a favorable safety and tolerability profile in a broad range of patients with relapsing forms of MS.[i] 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.

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 provides a new approach to treating 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 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 company 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 includes forward-looking statements, including statements about the potential benefits of TECFIDERA and analysis of the results of certain clinical studies. 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. These statements involve risks and uncertainties that could cause actual results or future results to differ materially from those reflected in such statements, including the occurrence of adverse safety events, unexpected results or concerns that may arise from additional data, clinical trials and studies, or analysis, unexpected regulatory actions or government regulation generally, and the other risks and uncertainties that are described in the Risk Factors section of our most recent annual or quarterly report and in other reports we have filed with the SEC. 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] TECFIDERA is approved in the European Union for relapsing-remitting multiple sclerosis

[2] Biogen data on file

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