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New Data Show Strong, Sustained Effects of TECFIDERA® (Dimethyl Fumarate) in Newly-Diagnosed and Early Disease Course Multiple Sclerosis Patients

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– TECFIDERA Significantly Reduced MS Inflammatory Disease Activity –

– Long-Term Efficacy and Safety of TECFIDERA Demonstrated in Six-Year Data from ENDORSE Study –

CAMBRIDGE, Mass.--(BUSINESS WIRE [2])--Biogen [3] (NASDAQ: BIIB) will present new data that reinforce the proven efficacy and well-established safety profile of TECFIDERA® (dimethyl fumarate) in a broad range of people with relapsing-remitting multiple sclerosis (RRMS) at the 31st Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in Barcelona, Spain (7-10 October). The data show that TECFIDERA significantly reduced multiple sclerosis (MS) relapses and delayed disability progression in patients who are newly diagnosed and those early in their disease course; these effects were sustained over six years of follow-up.

New data at ECTRIMS also include a post-hoc analysis in which TECFIDERA significantly reduced key inflammatory disease outcomes compared to glatiramer acetate (GA)[1] and, in a separate analysis, TECFIDERA demonstrated a favorable benefit-risk profile throughout six years of follow-up from the ENDORSE study.

“The benefits of taking a strong, efficacious therapy early in the disease course have been shown to improve a patient’s long-term prognosis when treatment is initiated before MS has advanced and caused irreparable damage,” said Ralf Gold, M.D., professor and chair of the Department of Neurology, St. Josef-Hospital/Ruhr-University Bochum. “The data at ECTRIMS demonstrate that patients initiating treatment with TECFIDERA early in their disease experienced significant reductions in relapse rates and disability progression over time compared to those taking placebo.”

Strong Efficacy in Early MS Patients
An analysis of the Phase 3 DEFINE and CONFIRM studies shows that TECFIDERA had significant effects on clinical outcomes in RRMS patients who initiated treatment early in their disease course, defined as those patients with a baseline Expanded Disability Status Scale (EDSS) score of ≤2.0 (indicating minimal to no disability). Compared to patients treated with placebo, TECFIDERA reduced annualized relapse rate (ARR) by 63 percent ($p<0.0001$) and reduced risk of 12-week confirmed disability progression by 40 percent ($p=0.0066$).

Reductions in Inflammatory Disease Outcomes
A post-hoc analysis of the MRI population from the Phase 3 CONFIRM study found that TECFIDERA significantly reduced key inflammatory disease outcomes compared to GA (20 mg subcutaneous daily injection). CONFIRM investigated TECFIDERA against placebo and included a reference comparator arm of GA versus placebo.

In this analysis, inflammatory disease activity was measured using a novel composite endpoint that included the presence of relapses, gadolinium-enhancing (Gd+) lesions and new or newly enlarging T2 lesions. An event was defined as a relapse, Gd+ lesion or new/newly enlarging T2 lesion occurring within a specified time interval over two years (weeks 0−24, 24−48, or 48−96). Patients were considered free of inflammatory disease activity if they did not experience an event within a given interval or any preceding intervals, and were evaluated for inflammatory disease activity as long as they were known to be at risk.

Results show that a higher proportion of TECFIDERA patients were free of inflammatory disease activity at all time intervals over two years:

- 36 percent of TECFIDERA patients compared to 29 percent of GA patients during weeks 0–24
- 34 percent of TECFIDERA patients compared to 23 percent of GA patients during weeks 24–48
- 21 percent of TECFIDERA patients compared to 16 percent of GA patients during weeks 48–96

and the overall HR (95% CI) for TECFIDERA compared to placebo was 0.60 (0.46–0.79; p=0.0002).

"Data continue to demonstrate that TECFIDERA reduces disability and relapse activity early in the disease course – meaning that it can help slow the progression of this debilitating disease, which is particularly important in newly-diagnosed or early disease course patients," said Gilmore O'Neill, M.D., vice president of Multiple Sclerosis Research and Development at Biogen. "With more than six years of clinical data supporting its strong, sustained efficacy and well-established safety profile, TECFIDERA has been used by more than 170,000 patients worldwide,[2] making it the most-prescribed oral MS medication globally."

Sustained Long-Term Efficacy and Well-Characterized Safety
Updated six-year data from an integrated post-hoc analysis of the Phase 3 DEFINE, CONFIRM and ENDORSE studies show long-term treatment with TECFIDERA resulted in strong and sustained effects on relapses and disability progression in newly-diagnosed patients (defined as those patients diagnosed with MS within one year prior to enrolling in DEFINE or CONFIRM and either treatment-naïve or previously treated with corticosteroids alone).

Throughout six years of study (two years in DEFINE or CONFIRM followed by four years in ENDORSE), the ARR for patients who started TECFIDERA treatment at the beginning of the study (n=85) remained low at 0.14 (0.10–0.19). In those patients who switched from placebo to TECFIDERA, the ARR was substantially reduced from 0.26 (0.18–0.37) from the placebo period (years zero to two) to 0.10 (0.06–0.16) when TECFIDERA treatment was received (years three to six), representing a 61 percent reduction of risk.

The proportion of patients with 24-week confirmed disability after six years of TECFIDERA treatment was 15.7 percent compared to 24.3 percent in those who switched to TECFIDERA treatment in year three. This represents a 49 percent reduction of disability risk (p=0.0397) at year six for those who started TECFIDERA treatment from the beginning, compared to those who started treatment later after two years of placebo.

Additional results from the ENDORSE extension study indicate that the favorable overall benefit-risk profile of TECFIDERA has remained consistent across all patients who received the therapy, including in those patients treated for up to eight years.

Data presentation details:

- Efficacy of Delayed-Release Dimethyl Fumarate in Early Multiple Sclerosis: Post-Hoc Analysis of the Phase 3 DEFINE and CONFIRM Studies According to Baseline Disability – *Poster P565 – Thursday, 8 October – 15:45-17:00 CEST*
- Longer-Term Follow-Up of the Efficacy of Delayed-Release Dimethyl Fumarate in Newly Diagnosed Patients with RRMS: An Integrated Analysis of DEFINE, CONFIRM, and ENDORSE – *Poster P564 – Thursday, 8 October – 15:45-17:00 CEST*
- Long-Term Follow-Up of the Safety of Delayed-Release Dimethyl Fumarate in RRMS: Interim Results from the ENDORSE Extension Study – *Poster P544 – Thursday, 8 October – 15:45-17:00 CEST*
- Efficacy of Delayed-Release Dimethyl Fumarate Versus Glatiramer Acetate on a Novel Composite Outcome Measure of Inflammatory Disease Activity: Post-Hoc Analysis of the CONFIRM Study – *Poster P1063 – Friday, 9 October – 15:30-17:00 CEST*

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. 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 DEFINE and CONFIRM
DEFINE (Determination of the Efficacy and safety of oral Fumarate IN relapsing-rEmitting 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; ARR; and disability progression as measured by EDSS. Safety and tolerability of TECFIDERA were also assessed.

CONFIRM (COmparator and aN oral Fumarate In Relapsing-remitting MS) 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, 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

lesions, while demonstrating a favorable benefit-risk profile in a broad range of patients with relapsing forms of MS. [3] 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 progressive multifocal leukoencephalopathy (PML) have been seen with TECFIDERA patients in the setting of severe and prolonged 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 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 [4].

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 http://www.biogen.com [5].

Safe Harbor
This press release includes forward-looking statements, including statements about the potential benefits of TECFIDERA in newly diagnosed and early onset MS patients. 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 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] Glatiramer acetate was an active reference comparator
[2] Combined post-marketing and clinical trials exposure to TECFIDERA as of August 31, 2015
[3] TECFIDERA is approved in the European Union for relapsing-remitting multiple sclerosis

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English

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