New Data from Phase 3 Studies Provide Additional Evidence Supporting Treatment Effect for Oral BG-12 (Dimethyl Fumarate) in Multiple Sclerosis

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– Interim Results from ENDORSE Extension Study Further Support Safety Profile from Pivotal Studies –

WESTON, Mass.--(BUSINESS WIRE)--Today Biogen Idec (NASDAQ: BIIB) announced new data from studies evaluating oral BG-12 (dimethyl fumarate), which provide further evidence supporting its strong clinical and radiological effects in people with relapsing-remitting multiple sclerosis (RRMS) and reinforce its favorable safety profile seen to date. These data were presented at the 28th Congress of the European Committee for the Treatment and Research of Multiple Sclerosis (ECTRIMS) in Lyon, France.

In a pre-specified analysis of integrated, or pooled, data from the Phase 3 DEFINE and CONFIRM studies, dimethyl fumarate showed statistically significant and clinically relevant effects in reducing multiple sclerosis (MS) relapses and progression of disability, as well as reductions in magnetic resonance imaging (MRI) measures of disease activity. In addition, interim safety data from a Phase 3 extension study indicate that continued exposure to dimethyl fumarate did not result in any new or worsening safety signals, and that its safety and tolerability profiles were consistent with previous studies.

“These data provide additional insight into the positive efficacy and safety results from our Phase 3 studies, showing there is a consistent beneficial effect with dimethyl fumarate in reducing MS relapses, brain lesions and disability,” said Alfred Sandrock, M.D., Ph.D., senior vice president, Development Sciences and chief medical officer of Biogen Idec. “If approved, dimethyl fumarate may provide a broad range of MS patients with an effective therapy that offers the ease of oral administration and an acceptable tolerability profile.”

Analyses of Pooled Phase 3 Efficacy Results

DEFINE and CONFIRM were randomized, double-blind studies that compared the efficacy and safety of dimethyl fumarate 240 mg, administered twice daily (BID) or three times daily (TID), to placebo over two years. CONFIRM also included a reference comparator of glatiramer acetate (GA; 20 mg subcutaneous daily injection). A pooled analysis of the efficacy data from more than 2,300 patients in these two studies was performed in order to provide the medical community with a more precise estimate of dimethyl fumarate’s treatment effects versus placebo on relapse, progression and MRI outcomes.

Analyses of the pooled clinical efficacy results of DEFINE and CONFIRM show that treatment with dimethyl fumarate led to significant reductions in MS relapses and disease progression. At two years compared to placebo, dimethyl fumarate significantly reduced:

- Annualized relapse rate (ARR) by 49 percent for both BID and TID ($p<0.0001$ for both)
- Proportion of patients who relapsed by 43 percent for BID and 47 percent for TID ($p<0.0001$ for both)
- Risk of 12-week confirmed disability progression, as measured by the Expanded Disability Status Scale (EDSS), by 32 percent for BID ($p=0.0034$) and 30 percent for TID ($p=0.0059$)

In MRI cohorts from DEFINE and CONFIRM, treatment with dimethyl fumarate significantly improved MRI outcomes over two years compared to placebo by reducing:

- Mean number of new or newly enlarging T2-hyperintense lesions by 78 percent for BID and 73 percent for TID ($p<0.0001$ for both)
- Mean number of new non-enhancing T1-hypointense lesions by 65 percent for BID and 64 percent for TID ($p<0.0001$ for both)
- Odds of having a greater number of gadolinium-enhancing (Gd+) lesions by 83 percent for BID and 70 percent for TID ($p<0.0001$ for both)

“These pooled results demonstrate that dimethyl fumarate had a significant effect on measures that MS patients are acutely aware of – the frequency of the relapses they experience and the progression of disability,” said Ralf Gold, Ph.D., professor/chair of the Department of Neurology at St. Josef-Hospital/Ruhr-University in Bochum, Germany. “As a physician who treats patients with MS, the strong results observed in the Phase 3 studies of dimethyl fumarate indicate that it may provide an attractive combination of efficacy, safety and tolerability.”

Pooled DEFINE and CONFIRM efficacy data are included in one platform and two poster presentations:

- *Clinical Effects of BG-12 in Subgroups of Patients with Relapsing-Remitting Multiple Sclerosis: An Integrated Analysis of the Phase 3 DEFINE and CONFIRM Studies* was available for viewing on Thursday, Oct. 11, 2012 from 3:30-5:00 p.m. CEST
- *Clinical Efficacy of BG-12 in Relapsing-Remitting Multiple Sclerosis: An Integrated Analysis of the Phase 3 DEFINE and CONFIRM Studies* will be presented by Prof. Ralf Gold on Friday, Oct. 12, 2012 at 2:40 p.m. CEST
- *Effects of BG-12 on Magnetic Resonance Imaging Outcomes in Relapsing-Remitting Multiple Sclerosis: An Integrated*

Analysis of the Phase 3 DEFINE and CONFIRM Studies will be available for viewing on Friday, Oct. 12, 2012 from 3:30-5:00 p.m. CEST

Pooled Safety Results

Safety and tolerability results were pooled from three placebo-controlled studies (DEFINE; CONFIRM; and a Phase 2 dose-ranging study) involving more than 2,400 patients who had received placebo or 240 mg of dimethyl fumarate twice or three times a day. These pooled data were consistent with results presented at previous medical conferences. The overall incidence of adverse events (AEs: 92% placebo, 95% BID, 93% TID) and serious adverse events (SAEs: 21% placebo, 18% BID, 15% TID) was similar for all treatment groups. The most common AEs associated with dimethyl fumarate treatment were flushing and gastrointestinal (GI) events; the incidence of these events was highest during the first month and decreased thereafter.

Mean lymphocyte counts decreased during the first year of dimethyl fumarate treatment and then plateaued, staying within normal limits throughout the entire treatment period. The incidence of hepatic and renal events was comparable among all study groups. The incidence of serious infections (≤2%) and malignancies (<1%) was low and balanced across the study groups. There were no opportunistic infections.

Pooled DEFINE and CONFIRM safety data are included in one poster presentation:

- *Safety and Tolerability of BG-12 in Patients with Relapsing-Remitting Multiple Sclerosis: An Integrated Analysis of the Placebo-Controlled Studies* was available for viewing on Thursday, Oct. 11 from 3:30-5:00 p.m. CEST

Interim Extension Study Safety Results

Positive interim safety data from ENDORSE, a dose-blind, multi-center, Phase 3 extension study evaluating the long-term safety and efficacy of dimethyl fumarate 240 mg BID and TID, will also be presented at the congress. At the time of analysis, 1,736 patients with RRMS who completed the DEFINE study or the CONFIRM study had been dosed in ENDORSE.

Patients who received two years of dimethyl fumarate in DEFINE and CONFIRM continued on the same dimethyl fumarate dose (BID or TID) in ENDORSE. Patients who had previously received placebo or GA (CONFIRM only) were randomized 1:1 to dimethyl fumarate 240 mg BID or TID.

At the time of analysis, more than half of the patients in ENDORSE had been followed for more than one year. Overall, the safety profile for those first exposed to dimethyl fumarate in ENDORSE was consistent with the safety results established in the DEFINE and CONFIRM studies. There were no new safety signals observed in patients who had previously been on dimethyl fumarate.

In ENDORSE, the incidence of serious infections was low (≤2%) in all treatment groups and there were no opportunistic infections. There was no increased risk of infection in patients treated long-term with dimethyl fumarate. The overall incidence of malignancies was low (<1%). The types and frequency of malignancies that were observed in the treatment groups were expected in the population under study, and no specific pattern of malignancies was observed.

These data are included in one poster presentation:

- *Long-Term Safety and Tolerability of Oral BG-12 (Dimethyl Fumarate) in Relapsing-Remitting Multiple Sclerosis: Interim Results from ENDORSE* will be available for viewing on Friday, Oct. 12 from 3:30-5:00 p.m. CEST (late-breaking news)

The data presented at ECTRIMS were included in Biogen Idec's regulatory submissions for dimethyl fumarate around the world.

For members of the media interested in more information and additional resources, please visit www.biogenidec.com/us_media_corner.

About DEFINE

DEFINE (**D**etermination of the **E**fficacy and safety of oral **F**umarate **IN** r**E**lapsing-remitting MS) was a global, randomized, double-blind, placebo-controlled, dose-comparison study to determine the efficacy and safety of dimethyl fumarate (240 mg, BID or TID) and enrolled 1,237 people with RRMS. The primary objective was to determine if dimethyl fumarate 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. Additional endpoints included the safety and tolerability of dimethyl fumarate. Detailed results from DEFINE were presented at the 5th Joint Triennial Congress of the European and Americas Committees on Treatment and Research in Multiple Sclerosis (ECTRIMS and ACTRIMS) in October 2011.

About CONFIRM

CONFIRM (**CO**mparator and a**N** oral **F**umarate **I**n **R**elapsing-remitting **M**S) was a global, randomized, double-blind, placebo-controlled, dose-comparison study to determine the efficacy and safety of dimethyl fumarate and enrolled 1,430 people with RRMS. The study evaluated two dose regimens of dimethyl fumarate, 240 mg BID and 240 mg TID, as well as a reference comparator of GA (20 mg subcutaneous daily injection). Both dimethyl fumarate and GA groups were evaluated versus placebo. The primary objective was to determine whether dimethyl fumarate was effective in reducing the rate of clinical relapses at two years. 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 in progression of disability as measured by EDSS. Safety and tolerability of dimethyl fumarate were also assessed. Detailed results from CONFIRM were presented at the 64th Annual Meeting of the American Academy of Neurology (AAN) in April 2012.

About ENDORSE

ENDORSE is an ongoing global, dose-blind extension study to determine the long-term safety and efficacy of dimethyl fumarate (240 mg, BID or TID). The study has enrolled 1,738 patients with RRMS who completed the DEFINE study or the CONFIRM study. Patients participating in ENDORSE will be followed for up to five years. The primary objective is to evaluate the long-term safety profile of dimethyl fumarate. Secondary objectives include: long-term efficacy of dimethyl fumarate on clinical outcomes and MS brain lesions on MRI scans; and effects of dimethyl fumarate on quality of life measurements. It is estimated that the ENDORSE study will be completed in 2016.

About Dimethyl Fumarate

Dimethyl fumarate, also known as BG-12, is an investigational oral therapy in late-stage clinical development for the treatment of RRMS, the most common form of MS. Dimethyl fumarate is the only currently known investigational compound for the treatment of RRMS that has experimentally

demonstrated activation of the Nrf-2 pathway.

Dimethyl fumarate is currently under review by regulatory authorities in the United States, European Union, Australia, Canada and Switzerland.

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.

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