The New England Journal of Medicine Publishes Pivotal Data Demonstrating Efficacy and Safety of Oral BG-12 (Dimethyl Fumarate) in Multiple Sclerosis

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Results of Phase 3 DEFINE and CONFIRM Studies Support Dimethyl Fumarate's Potential as a Strong Option for MS Treatment

WESTON, Mass.--(BUSINESS WIRE)--Today Biogen Idec (NASDAQ: BIIB) announced that detailed results from its two pivotal clinical trials evaluating oral BG-12 (dimethyl fumarate) for the treatment of multiple sclerosis (MS) were published in the Sept. 20, 2012 issue of *The New England Journal of Medicine* (NEJM).

Data from the Phase 3 DEFINE and CONFIRM studies show that dimethyl fumarate (240 mg), administered twice daily (BID) or three times daily (TID), demonstrated significant and clinically meaningful reductions in MS relapses and brain lesions in patients with relapsing-remitting multiple sclerosis (RRMS) compared to placebo, as well as showed benefit in slowing the progression of the disease. Dimethyl fumarate is currently under review by regulatory authorities in the United States, European Union, Australia, Canada and Switzerland.

"The publication of both dimethyl fumarate pivotal studies in NEJM is another achievement for this important investigational therapy," said Katherine Dawson, M.D., senior medical director, Biogen Idec Neurology Research and Development and Biogen Idec lead author on both dimethyl fumarate manuscripts in NEJM. "The data from its clinical development program consistently indicate that dimethyl fumarate may provide tangible benefits and address existing treatment needs of people living with MS. We are working closely with regulatory authorities across the globe with the aim of making the review of dimethyl fumarate as quick as possible."

DEFINE and CONFIRM Efficacy Results

Together, the DEFINE and CONFIRM manuscripts in NEJM summarize the positive Phase 3 clinical data set for dimethyl fumarate, which formed the foundation for its regulatory filings around the world.

DEFINE was a two-year global study that evaluated dimethyl fumarate (240 mg, BID or TID) compared to placebo in people with RRMS. Results showed that both dimethyl fumarate BID and TID met the study's primary endpoint by significantly reducing the proportion of patients who relapsed by 49 percent and 50 percent ($p<0.0001$ for both; reported in NEJM as <0.001 due to journal requirement that p-values smaller than 0.001 be reported as $p<0.001$), respectively, at two years compared to placebo. Both dosing regimens also met all secondary endpoints in the study.

"Because MS is a chronic disease, we look for treatment options that not only control relapses but also slow patients' disease progression for as long as possible," said Ralf Gold, Ph.D., professor/chair of the Department of Neurology at St. Josef-Hospital/Ruhr-University in Bochum, Germany, and lead author on the DEFINE manuscript in NEJM. "In DEFINE, dimethyl fumarate demonstrated efficacy, as well as positive safety and tolerability profiles, which is a very attractive combination for an MS treatment."

Like DEFINE, CONFIRM was a two-year global clinical trial that investigated dimethyl fumarate (240 mg, BID or TID) versus placebo in people with RRMS. The study also included an active reference comparator of glatiramer acetate (GA; 20 mg subcutaneous daily injection) versus placebo. Results showed that both dimethyl fumarate BID and TID met the study's primary endpoint by significantly reducing annualized relapse rate (ARR) by 44 percent and 51 percent ($p<0.0001$ for both; reported in NEJM as $p<0.001$ due to journal requirement that p-values smaller than 0.001 be reported as $p<0.001$), respectively, versus placebo at two years. In addition, both dosing regimens of dimethyl fumarate met all secondary relapse and magnetic resonance imaging (MRI) endpoints in the study. While not statistically significant, dimethyl fumarate showed a clinically meaningful reduction in 12-week confirmed disability progression as measured by the Expanded Disability Status Scale (EDSS).

The GA data versus placebo in CONFIRM were generally consistent with its product labeling.

"Results of the CONFIRM study were consistent with those of DEFINE, demonstrating that oral dimethyl fumarate significantly reduced MS disease activity compared to placebo and has a strong safety profile," said Robert J. Fox, M.D., medical director of the Mellen Center for Multiple Sclerosis at Cleveland Clinic and lead author on the CONFIRM manuscript in NEJM.* "I believe that these findings support the potential of oral dimethyl fumarate in RRMS for both treatment-naïve patients and those not tolerating or sub-optimally responding to currently available therapies."

** Dr. Robert Fox is a paid advisor for Biogen Idec for projects not related to dimethyl fumarate clinical development.*

The CONFIRM manuscript in NEJM also includes data from a post-hoc efficacy analysis that directly compared dimethyl fumarate to GA treatment. While CONFIRM was not designed for a formal statistical comparison of GA versus dimethyl fumarate treatment, this post-hoc analysis was included because it may provide helpful information regarding dimethyl fumarate's efficacy compared to an approved therapy for MS.

DEFINE and CONFIRM Safety Results

In DEFINE and CONFIRM, the safety profile for the dimethyl fumarate BID and TID treatment groups was similar. The overall incidence of adverse events (AEs), serious adverse events (SAEs) and AEs leading to study discontinuation was similar among the dimethyl fumarate and placebo groups in both studies.

In both studies, AEs that occurred more commonly with dimethyl fumarate treatment were flushing and gastrointestinal (GI) events. Flushing and GI events had the highest incidence in the first month of the study and decreased thereafter. The most frequently reported SAE across all treatment groups in both studies was MS relapse.

There was no increase in serious infections or malignancies in the dimethyl fumarate groups compared to placebo in either study. There were no opportunistic infections in the dimethyl fumarate groups. Laboratory analysis in both studies found mean white blood cell counts (WBC) and lymphocyte counts decreased during the first year in dimethyl fumarate-treated patients and then plateaued, remaining within the normal range throughout.

The full manuscripts, called “Placebo-Controlled Phase 3 Study of Oral BG-12 for Relapsing Multiple Sclerosis” (DEFINE) and “Placebo-Controlled Phase 3 Study of Oral BG-12 or Glatiramer in Multiple Sclerosis” (CONFIRM), can be found on the NEJM website at http://www.nejm.org.

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 new gadolinium-enhancing (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 BG-12 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 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 BG-12 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 Dimethyl Fumarate

Dimethyl fumarate, also known as BG-12, is an investigational oral therapy in late-stage clinical development for the treatment of relapsing-remitting multiple sclerosis (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.

In 2011 and 2012, Biogen Idec announced positive data from DEFINE and CONFIRM, two global, placebo-controlled Phase 3 clinical trials that evaluated 240 mg of dimethyl fumarate, administered either twice a day or three times a day, for two years. 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.

Safe Harbor

This press release includes forward-looking statements, including statements about the commercialization of BG-12 (dimethyl fumarate) in MS. These forward-looking statements may be accompanied by such words as "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," “potential,” "will" and other words and terms of similar meaning. You should not place undue reliance on these statements. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including obtaining regulatory approval, the occurrence of adverse safety events, product competition, the availability of reimbursement for our products, adverse market and economic conditions, problems with our manufacturing processes and our reliance on third parties, failure to comply with government regulation and possible adverse impact of changes in such regulation, our ability to protect our intellectual property rights and the cost of doing so, 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.

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