



Phase IIb Data Published in the Lancet Show That BG-12, Biogen Idec's Novel Oral Compound, Significantly Reduced Brain Lesions in Patients with Multiple Sclerosis

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CAMBRIDGE, Mass.--([BUSINESS WIRE](#))--Biogen Idec (NASDAQ: BIIB) today announced the publication of Phase IIb data showing that a 240 mg three-times-daily dose of the company's novel oral compound, BG-12 (BG00012, dimethyl fumarate), reduced the number of new gadolinium enhancing (Gd+) lesions by 69 percent in patients with relapsing-remitting multiple sclerosis (MS) when compared to treatment with placebo ($p < 0.0001$). The data also showed a 53 percent reduction in the mean number of T1-hypointense lesions and a 44 percent reduction in cumulative new Gd+ lesions in patients treated with BG-12 compared to treatment with placebo. The presence of Gd+ lesions is thought to indicate continuing inflammatory activity within the central nervous system. T1-hypointense lesions are associated with significant breakdown and loss of brain tissue. An ad hoc analysis conducted during the study showed a decrease in the likelihood of Gd+ lesions evolving into T1-hypointense lesions (black holes), warranting further clinical study into the potential neuroprotective and anti-inflammatory effects of BG-12. These results have been published in the October 25th issue of *The Lancet*.

BG-12 is the first compound that has been shown to activate the Nrf2 transcriptional pathway, which previous studies have shown defends against oxidative-stress induced neuronal death, protects the blood-brain barrier, and supports maintenance of myelin integrity in the central nervous system.

"The effects of BG-12 on inflammatory brain lesions, together with the corresponding safety data, strongly support further research in Phase III clinical studies to define its place in the future of relapsing-remitting MS treatment," said the study's primary investigator, Professor Ludwig Kappos, acting Chair of Neurology and Research Group Leader, Department of Biomedicine, University Hospital Basel, Switzerland. "Because of BG-12's unique mechanism of action and its oral administration, it could be valuable as a therapy for many MS patients and not just those who prefer to not initiate injectable treatments."

"Enhancing the body's normal cellular protection pathways while reducing inflammation appears to be a unique approach to this disease," said Michael Panzara, MD, MPH, Vice President, Chief Medical Officer of Neurology, Biogen Idec. "At Biogen Idec, we are continuing to invest and apply our expertise in MS with new research into novel compounds such as BG-12 to further improve the lives of people with this disease."

Phase IIb Data Demonstrate Positive Efficacy and Favorable Safety Profile for BG-12

In this study, patients treated with a 240 mg three-times-daily dose of BG-12 showed a reduction in the number of new Gd+ lesions by 69 percent at weeks 12 to 24, compared to treatment with placebo ($p < 0.0001$). The data also showed a 53 percent reduction in T1-hypointense lesions and a 44 percent reduction in cumulative new Gd+ lesions in patients treated with BG-12 compared to treatment with placebo. An ad hoc analysis demonstrated a reduced probability of the conversion of Gd+ lesions into T1-hypointense lesions, suggesting the possibility of additional neuroprotective benefits as observed in an earlier pilot study of ten patients with MS receiving oral fumaric acid ester therapy.

BG-12 also significantly reduced the number of new or enlarging T2-hyperintense lesions by 48 percent versus placebo, and 63 percent of patients given BG-12 had no new T2-hyperintense lesions, compared with 26 percent receiving placebo.

Though the study was not adequately powered to evaluate relapse endpoints, relapse rates in all BG-12 treatment groups decreased between the first and the second part of the study, which may indicate a delayed and increasing effect of BG-12 over time.

The most common, non-MS related adverse events that occurred more frequently in patients receiving BG-12 240 mg three times daily than those receiving placebo included flushing, headache, nausea, diarrhea, upper abdominal pain, hot flush, and abdominal pain. Flushing and gastrointestinal-related events decreased during the course of BG-12, especially during the first one-to-two months of treatment. Frequency of infection was low in all treatment groups and did not differ from that of the placebo group.

Data from this Phase IIb study lead the company to further pursue the development of BG-12. Two Phase III trials, DEFINE and CONFIRM, are currently underway evaluating the effect of BG-12 on measurements of clinical relapse, the progression of disability, and various MRI measures. BG-12 was granted Fast Track designation by the U.S. Food and Drug Administration earlier this year.

About the Study Design

In this Phase IIb randomized, double-blind, placebo-controlled, dose-ranging study, patients (n= 257), aged 18-55 years, with relapsing-remitting MS were randomly assigned to receive one of the following treatment regimens for 24 weeks: 120 mg of BG-12 once daily, 120 mg three times daily, 240 mg three times daily or placebo. The initial treatment period was followed by an extension period of 24 weeks for safety assessment, during which patients in the placebo group received BG-12 at 240 mg three times daily. The primary endpoint for the study was the total number of Gd+ lesions on brain MRI scans at weeks 12, 16, 18 and 24. Additional endpoints included cumulative number of new Gd+ lesions, new or enlarging T2-hyperintense lesions, new T1-hypointense lesions and annualized relapse rate. Safety and tolerability were also assessed. Results show that BG-12 met all of the study endpoints when given at the dose of 240 mg three times daily.

BG-12 Phase III Clinical Trials

The DEFINE (Determination of the Efficacy and safety of oral Fumarate IN relapsing-remitting MS) and CONFIRM (COMparator and aN oral Fumarate IN Relapsing-remitting MS) studies will include more than 2,000 total patients in North America, Europe and rest of world. DEFINE and CONFIRM are two-year, randomized, multi-center, double-blind, placebo-controlled, dose-comparison studies to determine the safety and efficacy of BG-12 in subjects with relapsing-remitting MS. CONFIRM will also include a glatiramer acetate (Copaxone®) reference comparator arm. Both DEFINE and CONFIRM are currently enrolling patients. For more information about DEFINE and CONFIRM, please email ms@dandersoncompany.com.

About Biogen Idec

Biogen Idec creates new standards of care in therapeutic areas with high unmet medical needs. Founded in 1978, Biogen Idec is a global leader in the

discovery, development, manufacturing and commercialization of innovative therapies. Patients in more than 90 countries benefit from Biogen Idec's significant products that address diseases such as lymphoma, multiple sclerosis, and rheumatoid arthritis. For product labeling, press releases and additional information about the company, please visit www.biogenidec.com.

Safe Harbor/Forward-Looking Statements

This press release contains forward-looking statements regarding BG-12. These statements are based on Biogen Idec's current beliefs and expectations. The commercial potential of BG-12 is subject to a number of risks and uncertainties, including the risk of meeting the end points in clinical trials, other unexpected delays or hurdles, and the uncertainty of obtaining regulatory approval. Drug development and commercialization involves a high degree of risk.

For more detailed information on the risks and uncertainties associated with Biogen Idec's drug development and other activities, see Item 1A "Risk Factors" in Biogen Idec's most recent Form 10-Q filing with the Securities and Exchange Commission. These forward looking statements speak only as of the date of this press release, and we assume no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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