Data at AAN Demonstrate Biogen's Leadership and Commitment to Innovation in MS

May 7, 2019

- *Updated results support lower risk of PML with extended interval dosing (EID; approximately every six weeks) for TYSABRI® (natalizumab) in patients in a real-world setting*
- *New interim data further support safety and efficacy of Biogen and Alkermes' investigational treatment, diroximel fumarate, to be marketed as VUMERITY™ if approved by the FDA*
- *Pooled Phase 3 data reinforce efficacy profile of TECFIDERA® (dimethyl fumarate)*

CAMBRIDGE, Mass., May 07, 2019 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) presented new data illustrating its ongoing commitment to improving care for people living with multiple sclerosis (MS) at the 71st annual meeting of the American Academy of Neurology (AAN) in Philadelphia (May 4–11). Data support the well-established therapies within Biogen's leading MS portfolio, TECFIDERA ® (dimethyl fumarate) and TYSABRI® (natalizumab). In addition, data show the potential of investigational drug VUMERITY™ (diroximel fumarate) as a meaningful therapy for relapsing MS and the implementation of more personalized treatment approaches for patients in the future through clinically useful biomarkers.

"We believe there are still significant opportunities to address the complex and often disparate needs of people living with this heterogeneous disease," said Alfred Sandrock, Jr., M.D., Ph.D., executive vice president and chief medical officer at Biogen. "Biogen is striving to meet those needs by making significant investments across our established MS portfolio with the aim of improving the treatment experience for patients, working to bring potentially meaningful new therapies to market and engaging in research that includes identifying biomarkers that can help standardize disease monitoring and inform future treatment decisions."

Comprehensive Data from Industry-Leading Portfolio of MS Therapies Aims to Address the Diverse Needs of MS Patients
New interim data – after a median of approximately one year of follow up – from the ongoing pivotal EVOLVE-MS-1 study support the effectiveness of Biogen and Alkermes' investigational treatment, diroximel fumarate, on clinical and radiological measures of disease activity in people with relapsing MS, particularly in newly diagnosed patients.

EVOLVE-MS-1 is an ongoing, open-label, two-year, Phase 3 study, planning to enroll approximately 1000 patients, to evaluate the safety and explore the efficacy of diroximel fumarate in patients with relapsing-remitting MS. New results in 696 MS patients on diroximel fumarate showed a significant reduction in the annualized relapse rate (ARR) by 79 percent over one year when compared to baseline, and by 82 percent in newly diagnosed patients. The mean number of gadolinium-enhancing (Gd+) lesions was reduced by 77 percent compared to baseline in the total population and by 96 percent in subgroup of newly diagnosed patients treated with diroximel fumarate. In safety analyses, no unexpected safety findings were observed during 15 months of follow up, and no opportunistic infections, including progressive multifocal leukoencephalopathy (PML), a serious brain infection, were associated with diroximel fumarate in the study to date. Diroximel fumarate is currently under review with the U.S. Food and Drug Administration (FDA) with a PDUFA (Prescription Drug User Fee Act) target action date in the fourth quarter of 2019. If approved, diroximel fumarate will be marketed under the brand name VUMERITY, which has been conditionally accepted by the FDA and will be confirmed upon approval.

Committed to further understanding the benefit-risk profile of natalizumab, Biogen presented updated safety analyses evaluating extended interval dosing (EID) of approximately every six weeks for natalizumab compared to the approved every four-week dosing. The updated retrospective analysis supports the view that EID is associated with a significantly lower risk of PML compared to the approved every four-week dosing regimen. As announced earlier this year, Biogen has initiated the ongoing Phase 3b NOVA study (NCT03689972) to assess the efficacy of every six-week natalizumab dosing intervals in people with relapsing-remitting MS.

To understand changes in brain volume in patients treated with TECFIDERA, researchers re-analyzed pooled images from the Phase 3 DEFINE and CONFIRM studies. Brain volume loss progresses faster in people with MS and correlates with disability progression and cognitive impairment. The re-analysis presented at AAN shows that, consistent with TECFIDERA's effects on other measures of MS disease activity, the treatment significantly slowed the rate of whole brain volume loss by 35.9 percent during the second year of treatment compared to placebo.

Biomarker Research Nears Clinical Utility to Drive More Personalized Medicine in MS
Biogen has been engaged in collaborative research efforts to aid in the development of confirmed biomarkers, such as neurofilament, to move toward a precision management approach in treating MS and other neurodegenerative diseases. Data previously presented has demonstrated the clinical relevance of serum neurofilament light (sNfL) levels to predict disease severity and monitor treatment response in MS patients. New findings from the ASCEND study of natalizumab in secondary progressive MS (SPMS) lend further support to the potential clinical relevance of sNfL levels and demonstrate natalizumab's ability to reduce sNfL concentrations compared to placebo in patients with SPMS with or without acute inflammatory activity.

Featured Data Presentation Details:

Platform Presentations

- Serum Neurofilament Light (sNfL) for Disease Prognosis and Treatment Monitoring in Multiple Sclerosis Patients: Towards Implementation into Clinical Care – *Platform S26.001 – Tuesday, May 7, 1:00 p.m. ET*
- Reduced Risk of Progressive Multifocal Leukoencephalopathy (PML) Associated With Natalizumab Extended Interval Dosing (EID): Updated Analysis of the TOUCH® Prescribing Program Database – *Platform S26.006 – Tuesday, May 7, 1:55 p.m. ET*

Posters

- Diroximel Fumarate (DRF) in Patients With Relapsing-Remitting Multiple Sclerosis: Interim Efficacy and Safety Results

From the Phase 3 EVOLVE-MS- Study – *Poster P3.2-060 -- Tuesday, May 7, 11:30 a.m. – 6:30 p.m. ET*

- Effects of Dimethyl Fumarate on Brain Volume Change in Relapsing-remitting Multiple Sclerosis: A Pooled Analysis of the Phase 3 DEFINE and CONFIRM Studies – *Poster P3.2-064 – Tuesday, May 7, 11:30 a.m. – 6:30 p.m. ET*
- Evaluating the Efficacy and Safety of 6-Week Extended Interval Dosing of Natalizumab via a Prospective, Controlled, Randomized, Open-Label, Rater-Blinded Phase 3b Study – *Poster P3.2-095 – Tuesday, May 7, 11:30 a.m. – 6:30 p.m. ET*

About Tecfidera® (dimethyl fumarate)
TECFIDERA is the most prescribed oral medication for relapsing multiple sclerosis (MS) in the world and has been shown to reduce the rate of MS relapses, slow the progression of disability and impact the number of MS brain lesions, while demonstrating a well-characterized safety profile in people with relapsing forms of MS. TECFIDERA is approved in 69 countries and more than 385,000 patients have been treated with DMF, representing more than 710,000 patient-years of exposure across clinical trial use and patients prescribed TECFIDERA. Of these, 6,335 patients (12,985 patient-years) were from clinical trials.[i] TECFIDERA is indicated in the U.S. for the treatment of patients with relapsing forms of MS, and is approved in the European Union for relapsing-remitting MS.

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, a rare opportunistic viral infection of the brain which has been associated with death or severe disability, have been seen with TECFIDERA patients in the setting of prolonged lymphopenia although the role of lymphopenia in these cases is uncertain. Other serious side effects include a decrease in mean lymphocyte counts during the first year of treatment, which then plateaued, and liver function abnormalities, which resolved upon treatment discontinuation. In clinical trials, the most common adverse events associated with TECFIDERA were flushing and gastrointestinal (GI) events.

Please click here for Important Safety Information and full Prescribing Information, including Patient Information for TECFIDERA in the U.S., or visit your respective country's product website.

About Tysabri® (natalizumab)
TYSABRI is a well-established relapsing multiple sclerosis (RMS) treatment that has been proven in clinical trials to slow physical disability progression, reduce the formation of new brain lesions and cut relapses. TYSABRI is approved in 80 countries, and nearly 200,000 people worldwide have been treated with TYSABRI, with over 725,000 patient-years of experience, based on clinical trials and prescription data.[ii] In the U.S., TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of MS. In the European Union, it is indicated as single disease modifying therapy (DMT) in adults with highly active relapsing-remitting MS (RRMS) for patients despite a full and adequate course of treatment, with at least one DMT or patients with rapidly evolving severe RRMS.

TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), a rare opportunistic viral infection of the brain which has been associated with death or severe disability. Risk factors that increase the risk of PML are the presence of anti-JC virus antibodies, prior immunosuppressant use and longer TYSABRI treatment duration. Patients who have all three risk factors have the highest risk of developing PML.

TYSABRI also increases the risk of developing encephalitis and meningitis caused by herpes simplex and varicella zoster viruses, and serious, life-threatening and sometimes fatal cases have been reported in the post-marketing setting in MS patients receiving TYSABRI. Clinically significant liver injury, including acute liver failure requiring transplant, has also been reported in the post-marketing setting. Other serious adverse events that have occurred in TYSABRI-treated patients include hypersensitivity reactions (e.g., anaphylaxis) and infections, including opportunistic and other atypical infections.

Please click here for Important Safety Information, including **Boxed Warning**, and full Prescribing Information, including Medication Guide for TYSABRI in the U.S., or visit your respective country's product website.

About Diroximel Fumarate
Diroximel fumarate (BIIB098) is a novel oral fumarate candidate in development for the treatment of relapsing forms of MS. Diroximel fumarate is designed to rapidly convert to monomethyl fumarate in the body and with a distinct chemical structure, may have the potential to offer differentiated gastrointestinal (GI) tolerability as compared to dimethyl fumarate. Alkermes is conducting the EVOLVE-MS-2 study in patients with relapsing-remitting (RRMS), a five-week, head-to-head study versus dimethyl fumarate to evaluate GI tolerability in addition to the EVOLVE-MS-1 study. Diroximel fumarate is currently under review with the U.S. Food and Drug Administration (FDA) with a PDUFA (Prescription Drug User Fee Act) target action date in the fourth quarter of 2019. Diroximel fumarate will be marketed under the brand name VUMERITY, which has been conditionally accepted by the FDA and will be confirmed upon approval.

About Biogen
At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops, and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative diseases as well as related therapeutic adjacencies. One of the world's first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Kenneth Murray, and Nobel Prize winners Walter Gilbert and Phillip Sharp, and today has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first and only approved treatment for spinal muscular atrophy, and is focused on advancing neuroscience research programs in MS and neuroimmunology, Alzheimer's disease and dementia, movement disorders, neuromuscular disorders, acute neurology, neurocognitive disorders, pain, and ophthalmology. Biogen also commercializes biosimilars of advanced biologics.

We routinely post information that may be important to investors on our website at www.biogen.com. To learn more, please visit www.biogen.com and follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

Biogen Safe Harbor
This news release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to the potential benefits, safety and efficacy of TECFIDERA, TYSABRI and diroximel fumarate; the results of certain real-world data; potential regulatory approval and the timing thereof; clinical trial results and plans; our research and development program for the treatment of MS; the identification and treatment of MS; the potential of our commercial business and pipeline programs, including diroximel fumarate; the anticipated benefits and potential of our collaboration arrangements with Alkermes; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "except," "forecast," "goal," "intend," "may," "plan," "possible," "potential," "will," "would" and other words and terms of similar meaning. 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. Results in early stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including

without limitation the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis; risks of unexpected costs or delays; regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates, including diroximel fumarate, or expansion of product labeling; actual timing and content of submissions to and decisions made by the regulatory authorities regarding our drug candidates, including diroximel fumarate; regulatory submissions may take longer or be more difficult to complete than expected; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, including diroximel fumarate; the risk that we may not fully enroll our clinical trials or enrollment will take longer than expected; unexpected concerns may arise from additional data, analysis or results obtained during our clinical trials; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; uncertainty of success in the development and potential commercialization of VUMERITY; risks relating to the potential launch of VUMERITY, including preparedness of healthcare providers to treat patients, the ability to obtain and maintain adequate reimbursement for VUMERITY and other unexpected difficulties or hurdles; product liability claims; and third party collaboration risks. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from our expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in our most recent annual or quarterly report and in other reports we have filed with the U.S. Securities and Exchange Commission. These statements are based on our current beliefs and expectations and speak only as of the date of this news release. We do not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments, or otherwise.

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[i] Combined post-marketing data based on prescriptions and clinical trials exposure to TECFIDERA as of January 31, 2019.

[ii] Global Natalizumab (TYSABRI) Postmarketing PML Update, March 2019.