Biogen Advances Research to Improve Outcomes for Patients With Multiple Sclerosis

October 11, 2018

- Evidence supports potential of serum neurofilament light (sNfL) as clinically useful biomarker in MS; Biogen and Siemens Healthineers collaborate to develop sNfL blood test
- Real-world data add to the large body of evidence establishing the long-term effectiveness of TECFIDERA and TYSABRI, including in newly diagnosed patients
- MS PATHS, generating standardized data from more than 13,000 people with MS, uses new tools to objectively monitor for cognitive changes

CAMBRIDGE, Mass., Oct. 11, 2018 (GLOBE NEWSWIRE) -- Through its research initiatives, Biogen Inc. (Nasdaq: BIIB) aims to identify new ways to manage and monitor multiple sclerosis (MS) disease progression and provide physicians with real-world evidence to help inform treatment decisions. Data show serum neurofilament light (sNfL) is a potential biomarker of disease activity and treatment response, and results from MS PATHS (Multiple Sclerosis Partners Advancing Technology and Health Solutions) support the use of technology to broadly monitor for clinically important outcomes, including cognitive changes. New analyses of ongoing studies continue to support the long-term benefits of TECFIDERA® (dimethyl fumarate) and TYSABRI® (natalizumab), particularly when initiating treatment early within the disease course. These findings are being presented at the 34th Congress of the European Committee for Treatment and Research in MS in Berlin, Germany (ECTRIMS; October 10-12).

“Biogen remains committed to investing in MS and pursuing research efforts to advance our understanding of the disease, including aspects that matter most to patients,” said Michael Ehlers, executive vice president, research & development at Biogen. “We are generating data that have led to the development of new tools for everyday clinical practice and which inform personalized decisions with the aim of improving patient outcomes.”

Biomarker Could Guide MS Treatment Decisions
Biogen is engaged in research to evaluate sNfL, a protein that reflects neuronal damage and is elevated in the blood of people with MS, as a biomarker of disease activity. Results from a retrospective analysis of more than 1,000 patients support the clinical relevance of sNfL levels in the blood to predict disease severity and monitor treatment response in MS patients. Data indicate that sNfL levels above a certain threshold are associated with ongoing disease activity and negative clinical and radiologic outcomes, such as more disability progression and brain atrophy. Researchers also found that introducing disease-modifying therapies significantly reduced sNfL levels, and greater reduction was associated with better treatment outcomes.

“Our research suggests that serum neurofilament light is a promising biomarker that may predict a person’s disease course and help guide treatment decisions in MS,” said Peter Calabresi, M.D., director of the division of neuroimmunology and neuro-infectious diseases at the Johns Hopkins University School of Medicine. “These findings support sNfL as a clinically useful biomarker to help predict whether a person with MS is likely to have a fast-progressing or milder disease course. They also open the possibility of using a simple blood test to monitor whether a patient is responding to a specific treatment. The strong predictive power of sNfL may ultimately provide physicians with additional information beyond what is currently measured by MRIs to help guide treatment decisions.”

Biogen is working to transition these results into a potentially valuable resource for clinical practice, and has expanded its collaboration with Siemens Healthineers to develop an sNfL blood test as an additional tool to monitor MS. A highly sensitive, robust and validated assay will allow physicians to measure sNfL levels in the blood of MS patients with the goal of better understanding disease activity and monitoring treatment response.

Real-World Evidence Reinforces Long-Term Effectiveness of TECFIDERA and TYSABRI
Biogen recognizes the importance of real-world evidence to help guide decisions in clinical practice and optimize patient care. The company continues to evaluate its leading MS therapies, TECFIDERA and TYSABRI, to better understand the benefits of using these treatments, including when initiated early within the disease and treatment course.

Results from the ENDORSE study demonstrate that the clinical benefits of TECFIDERA in reducing MS relapses and disability progression in newly diagnosed patients were maintained throughout nine years of continuous TECFIDERA treatment, with relapse rates remaining low and more than 90 percent of patients maintaining walking abilities. An analysis from the TYSABRI Observational Program (TOP), the largest ongoing, real-world study of TYSABRI-treated patients, reinforces the long-term safety and consistent effectiveness of TYSABRI over 10 years, especially for patients with minimal or mild disability and those who were previously treated with fewer disease-modifying therapies.

New Technologies Help Monitor and Manage MS
Through MS PATHS, a collaboration with 10 leading MS centers in Europe and the U.S., Biogen continues to leverage technology in routine care to collect clinical, MRI and biologic data from patients in real time, at the point of care. Using an iPad-based assessment, researchers are able to broadly monitor for changes in motor, visual and cognitive function. Cognitive deficits affect more than half of people living with MS yet have not been regularly assessed in clinical practice and can be difficult to quantify.[1] New MS PATHS data demonstrate that cognitive decline is as prevalent as physical decline in people with MS but can occur independently from physical symptoms. These results underscore the importance of monitoring cognition in routine care and the need for effective treatment strategies for cognitive changes in MS.

To help physicians outside of the MS PATHS network easily assess cognition in their patients, Biogen has developed CogEval, a free app available to healthcare providers in the U.S., Europe, Canada, Japan, Australia and New Zealand. Like the Processing Speed Test used in MS PATHS, CogEval is modeled after and validated against the Symbol Digit Modalities Test, regarded by many experts as the gold standard of MS cognitive screening tests. CogEval provides a two-minute, iPad-based assessment of cognitive function that depends on attention, psychomotor speed, visual processing and working memory.

“Through MS PATHS, Biogen is merging technology with routine care to broadly monitor for MS functional abilities, including cognition – a clinically meaningful aspect of disease progression on patients’ daily lives,” said Alfred Sandrock, Jr., M.D., Ph.D., executive vice president and chief medical officer at Biogen. “We are pleased to bring this technology to physicians outside of the MS PATHS network through the development of innovative solutions like the CogEval app, with the aim of helping physicians more easily assess cognitive function in clinical practice.”

Featured data presentation details:

- Temporal Relationship of Serum Neurofilament Light Levels and Radiological Disease Activity in Patients with Multiple Sclerosis – *Poster P532 – Wednesday, 10 October, 17:00-19:00 CET*
- Prevalence of Isolated Cognitive Decline in a Large, Heterogeneous Multiple Sclerosis Population – *Poster P517 – Wednesday, 10 October, 17:00-19:00 CET*
- Serum Neurofilament Light (sNfL) for Disease Prognosis and Treatment Monitoring in Multiple Sclerosis Patients: Is it Ready for Implementation into Clinical Care? – *Platform 5 – Thursday, 11 October, 11:16-11:28 CET*
- Real-world Data from Over 10 years in the TYSABRI® Observational Program: Long-term Safety and Effectiveness of Natalizumab in Relapsing-remitting Multiple Sclerosis Patients – *Poster P908 – Thursday, 11 October, 17:15-19:15 CET*
- Delayed-release Dimethyl Fumarate Demonstrates Sustained Efficacy over Nine Years in Newly Diagnosed Patients with Relapsing-Remitting Multiple Sclerosis – *Poster P920 – Thursday, 11 October, 17:15-19:15 CET*
- Benchmarks of Manual Dexterity and Walking Speed in a Large, Representative Patient Population – *Poster P1018 – Friday, 12 October, 12:15-14:15 CET*

About TECFIDERA®
TECFIDERA is an oral therapy for relapsing forms of MS, including relapsing-remitting MS, the most common form of MS. More than 340,000 patients have been treated with TECFIDERA worldwide with over 625,000 patient-years of experience, based on clinical trials and prescription data.[2] TECFIDERA has been proven to reduce the rate of MS relapses, slow the progression of disability and impact the number of MS brain lesions, while demonstrating a favorable benefit-risk profile in people with relapsing forms of MS, notably newly diagnosed and early switch populations. In clinical trials, the most common adverse events associated with TECFIDERA were flushing and gastrointestinal (GI) events. Other 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. 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), 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 moderate to severe lymphopenia.

The efficacy and safety of TECFIDERA have been studied in a large, global clinical program, which includes an ongoing long-term extension study.

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®
TYSABRI is a disease modifying therapy (DMT) approved in more than 80 countries including the U.S., the European Union, Canada, Australia and Switzerland. 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 DMT in adults with highly active relapsing-remitting MS (RRMS) for patients with highly active disease activity despite a full and adequate course of treatment with at least one DMT or patients with rapidly evolving severe RRMS. TYSABRI is proven effective, with over 10 years of experience in treating RRMS, and more than 190,800 people treated worldwide and over 658,169 patient-years of experience.[3]

TYSABRI is a monoclonal antibody that selectively binds to α4-integrin and is thought to interrupt the activity of inflammatory cells in MS patients by blocking the interaction between α4β1-integrin and vascular cell adhesion molecule-1. Disruption of these molecular interactions prevents transmigration of leukocytes across the endothelium into inflamed parenchymal tissue. The specific mechanism(s) by which TYSABRI exerts its effects in MS have not been fully defined.

TYSABRI has advanced the treatment of MS patients with its proven ability to slow the progression of disability, reduce relapse rates and impact the number of MRI brain lesions with a well-characterized safety profile. Data from the Phase 3 AFFIRM trial, which were published in the *New England Journal of Medicine*, showed that at two years, TYSABRI treatment led to a 68 percent relative reduction ($p<0.001$) in the annualized relapse rate when compared with placebo and reduced the relative risk of disability progression by 42 to 54 percent (12-24-week sustained respectively, both $p<0.001$).

TYSABRI increases the risk of 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-JCV antibodies, prior immunosuppressant use and longer TYSABRI treatment duration. Patients who have all three risk factors have the highest risk of developing PML. TYSABRI increases the risk of developing encephalitis and meningitis caused by herpes simplex and varicella zoster viruses and clinically significant liver injury has also been reported in the post-marketing setting. Serious, life-threatening and sometimes fatal cases have been reported in the post-marketing setting in MS patients receiving TYSABRI. 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. Clinically significant liver injury has also been reported in the post-marketing setting.

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 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. 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 Alzheimer's disease and dementia, multiple sclerosis and neuroimmunology, movement disorders, neuromuscular disorders, pain, ophthalmology, neuropsychiatry and acute neurology. Biogen also manufactures and 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 press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, about clinical studies and real-world data related to TECFIDERA, TYSABRI and the identification and treatment of MS; the potential benefits, safety and efficacy of TECFIDERA and TYSABRI; the identification and treatment of MS; the potential of our commercial business, including TECFIDERA and TYSABRI; the anticipated benefits and potential of our collaboration arrangement with Siemens Healthineers; and risks and uncertainties associated with drug development and commercialization. These statements may be identified by words such as "aim,"

“anticipate,” “believe,” “could,” “estimate,” “expect,” “goal,” “forecast,” “intend,” “may,” “plan,” “possible,” “potential,” “will” 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: unexpected concerns that may arise from additional data, analysis or results obtained during our clinical trials; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates or expansion of product labeling; the occurrence of adverse safety events; risks of unexpected costs or delays; we may encounter other unexpected hurdles; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; uncertainty as to whether the anticipated benefits and potential of Biogen’s collaboration arrangement with Siemens Healthineers can be achieved; 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 press 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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[1] Multiple Sclerosis International Federation (MSIF). 2013. *MS in focus: MS and cognition.* Available at: https://www.msif.org/wp-content/uploads/2014/09/MS-in-focus-22-Cognition-English1.pdf. Last accessed: Sept. 25, 2018.

[2] Combined post-marketing data based on prescriptions and clinical trials exposure to TECFIDERA as of 31 July 2018.

[3] Global Natalizumab (TYSABRI) Postmarketing PML Update, August 2018.