New Data at AAN 2022 Highlight Real-World Evidence from Biogen's MS Portfolio and Emerging Research on Disease Progression

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- *Data from NOVA study further support the efficacy and safety of natalizumab IV when administered every six weeks as compared to the approved every four-week dosing*
- *Additional real-world data affirm high rates of persistence and adherence for VUMERITY® (diroximel fumarate)*
- *Early research investigates the potential of machine learning to predict MS disease progression from brain MRI scans*

CAMBRIDGE, Mass., April 04, 2022 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced new data from its industry-leading portfolio of multiple sclerosis (MS) therapies being presented at the American Academy of Neurology (AAN) 2022 Annual Meeting. The presentations include new real-world, long-term data on TYSABRI® (natalizumab), as well as persistence and adherence learnings with VUMERITY® (diroximel fumarate). Additional presentations highlight the use of digital tools to potentially predict MS disease progression. These data build on ongoing work to advance the understanding and treatment of serious neurological and neurodegenerative diseases, and highlight Biogen's commitment to science that strives to address the diverse needs of people living with MS.

"Through our close work with the MS community, we have gained a strong appreciation for the diverse needs of people living with MS and continue to pursue research that is important to patients, including these new data on TYSABRI and VUMERITY," said Maha Radhakrishnan, M.D., Chief Medical Officer at Biogen. "Additional presentations at AAN demonstrate our focus on advancing neuroscience research, including the ambitious work underway through Biogen Digital Health to identify digital health solutions aimed at improving the diagnosis and treatment of neurological conditions."

Real-World and Clinical Trial Data Show Consistent Profile With Long-Term TYSABRI Use and Every-Six Week Administration
Two presentations contribute to the understanding of extended interval dosing (EID) with intravenous (IV) natalizumab in real-world and clinical trial settings.

- An updated analysis of the U.S. TOUCH® (TYSABRI Outreach: Unified Commitment to Health) database as of June 30, 2021, confirms results from earlier analyses, which found that EID with IV administration of natalizumab is associated with a significantly lower risk of progressive multifocal leukoencephalopathy (PML) than the approved every four-week (Q4W) dosing. In the updated analysis, which included more patients and longer exposures, EID was associated with a significant 87% reduction (hazard ratio 0.127; P<0.0001) in the probability of PML in comparison to the approved Q4W dose.
- Primary results from the Phase 3b NOVA study of every six-week (Q6W) IV dosing with natalizumab were also presented during a platform session, showing that Q6W administration of natalizumab maintains control of MS disease activity in patients who switched to Q6W after at least one year of disease stability on the approved Q4W IV dosing schedule. Topline data were first reported in August 2021, and additional results were shared at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) annual congress last year. The approved dose of TYSABRI is 300mg on a Q4W dosing regimen.

In addition to the data presented on Q6W IV dosing with natalizumab, a new analysis of the observational STRIVE study using the approved Q4W IV TYSABRI dosing schedule found that treatment-naïve patients with early relapsing-remitting multiple sclerosis (RRMS) had improved clinical outcomes in comparison with patients who had received prior disease-modifying therapies (DMTs). These findings provide useful information on the added clinical benefit that initiating treatment early in the disease course with TYSABRI may provide. At four years, the cumulative probability of 24-week confirmed disability worsening (CDW) was significantly lower in treatment-naïve patients than in patients with prior DMT treatment (11.5% vs 29.0%; P=0.0015).

Real-World Analyses Further Demonstrate High Rates of Persistence and Adherence for VUMERITY
In the treatment of MS, high levels of adherence and persistence with DMTs are associated with improved clinical outcomes and reduced treatment costs.[1] Two claims analyses from AcariaHealth Specialty Pharmacy Program and Optum showed high rates of persistence and adherence with VUMERITY, consistent with clinical trial experience and further supporting VUMERITY as a well-tolerated oral fumarate option due to its gastrointestinal (GI) tolerability profile.

- A retrospective analysis of the AcariaHealth Specialty Pharmacy Program included 1,143 patients who initiated therapy with VUMERITY between Dec. 1, 2019, and Jan. 30, 2021. Persistence as measured by the overall estimated proportion of patients remaining on VUMERITY at 16 months was 82.3%; 4.5% discontinued VUMERITY due to GI side effects. Adherence, as measured by proportion of days covered (PDC), was 90.8%, and 85.4% of patients achieved a PDC ≥80%. Consistent findings were also observed in a subgroup of 433 patients who switched from TECFIDERA® (dimethyl fumarate) to VUMERITY.
- An Optum claims analysis included 1,885 patients with at least one MS-related claim between Oct. 1, 2019, and March 31, 2021: 224 were treated with VUMERITY, 746 with TECFIDERA, 601 with teriflunomide, 182 with fingolimod and 132 with siponimod. Persistence and adherence rates for VUMERITY after 90 days were 84% and 88%, respectively, consistent with or higher than those for other DMTs; 79% of patients achieved a PDC ≥80%.

Biogen Continues Pursuit of Innovation in MS With Digital Health Research
Multiple presentations support Biogen's commitment to delivering innovative approaches to reframe the care and treatment of MS, including the development of digital tools to help refine the assessment of disease progression by using cutting-edge computer vision applied to brain magnetic

resonance imaging (MRI) scans. Several abstracts highlight early work using machine learning to predict MS lesion formation and detect slowly expanding lesions (SELs). This research is designed to help better understand MS disease heterogeneity by unravelling the mechanisms of acute lesion formation and chronic lesion evolution, which could in the future help inform clinical trial design and, ultimately, improve patient care.

"This is an exciting time in MS research as we see the confluence of medical and computational science," said Shibeshih Belachew, M.D. PhD., Head of Science, Biogen Digital Health. "These presentations on novel medical image computing tools and advanced algorithmic solutions provide an early vision for predicting disease progression, driving even greater steps toward more precise and personalized care of people living with MS."

Data Presentations Featured at AAN:

- Natalizumab Extended Interval Dosing (EID) Is Associated with a Reduced Risk of Progressive Multifocal Leukoencephalopathy (PML) Compared with Every-4-Week (Q4W) Dosing: Updated Analysis of the TOUCH® Prescribing Program Database – P13.010 – Wednesday, April 6, 8-9 a.m. PDT
- Primary Results of NOVA: a Randomized Controlled Study of the Efficacy of 6-Week Dosing of Natalizumab Versus Continued 4-Week Treatment for Multiple Sclerosis – S14.005 – Monday, April 4, 4:18-4:30 p.m. PDT
- Effectiveness of Natalizumab Treatment in Patients with Early Relapsing-Remitting Multiple Sclerosis (RRMS) Who Were Treatment-Naive Versus Those Who Had Prior Disease-Modifying Therapy (DMT) Use – P6.006 - Sunday, April 3, 5:30-6:30 p.m. PDT
- Updated Real-World Analysis Affirms the High Persistence and Adherence Observed with Diroximel Fumarate in Patients with Multiple Sclerosis – P9.007 – Monday, April 4, 5:30-6:30 p.m. PDT
- Diroximel Fumarate (DRF) Has High Rates of Real-World Adherence and Persistence in Patients with Multiple Sclerosis (MS): Retrospective Claims Analysis – P9.008 – Monday, April 4, 5:30-6:30 p.m. PDT
- Diroximel Fumarate in Patients with Relapsing-Remitting Multiple Sclerosis: Interim Safety and Efficacy Results from the Phase 3 EVOLVE-MS-1 Study – P7.008 – Monday, April 4, 8-9 a.m. PDT
- Machine Learning-Based Detection of Slowly Expanding Lesions Using Radiomic Features from Cross-sectional Brain MRI – S26.004 – Wednesday, April 6, 1:36-1:48 p.m. PDT
- Machine Learning-Based Prediction of New Multiple Sclerosis Lesion Formation Using Radiomic Features from Pre-Lesion Normal Appearing White Matter – S26.009 – Wednesday, April 6, 2:36-2:48 p.m. PDT
- Exploring the Utility of MRI-Based 'SuStaIn' Disease Subtyping for Precision Medicine in Relapsing and Secondary Progressive MS – P15.002 – Wednesday, April 6 at 5:30-6:30 p.m. PDT

About TYSABRI® (natalizumab)
TYSABRI is a well-established relapsing multiple sclerosis (RMS) treatment indicated for relapsing forms of MS in adults 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 over 240,000 people worldwide have been treated with TYSABRI, with over 970,000 patient-years of experience, based on clinical trials and prescription data.[2]

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. When initiating and continuing treatment with TYSABRI, physicians should consider whether the expected benefit of TYSABRI is sufficient to offset this risk.

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), a decrease in lymphocyte counts 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 VUMERITY® (diroximel fumarate)
VUMERITY is an oral fumarate with a distinct chemical structure from TECFIDERA® (dimethyl fumarate), approved in the U.S. for the treatment of relapsing forms of multiple sclerosis in adults, to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease. Once in the body, VUMERITY rapidly converts to monomethyl fumarate, the same active metabolite of dimethyl fumarate. VUMERITY is approved in more than 30 countries, and more than 20,000 patients have been treated with it, representing more than 15,000 patient-years of exposure across clinical trial use and patients prescribed VUMERITY. [3]

VUMERITY is contraindicated in patients with known hypersensitivity to diroximel fumarate, dimethyl fumarate or to any of the excipients of VUMERITY; and in patients taking dimethyl fumarate. Serious side effects for VUMERITY are based on data from dimethyl fumarate (which has the same active metabolite as VUMERITY) and include anaphylaxis and angioedema, progressive multifocal leukoencephalopathy, which is a rare opportunistic viral infection of the brain that has been associated with death or severe disability, a decrease in mean lymphocyte counts during the first year of treatment, herpes zoster and other serious infections, liver injury and flushing. The most common adverse events, obtained using data from dimethyl fumarate (which has the same active metabolite as VUMERITY), were flushing, abdominal pain, diarrhea and nausea.

Please click here for Important Safety Information and full Prescribing Information, including Patient Information for VUMERITY in the U.S.

About TECFIDERA® (dimethyl fumarate)
TECFIDERA, a treatment for relapsing forms of multiple sclerosis (MS) in adults, is the most prescribed oral medication for relapsing 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 560,000 patients have been treated with it, representing more than 1,100,000 patient-years of exposure across clinical trial use and patients prescribed TECFIDERA.[4]

TECFIDERA is contraindicated in patients with a known hypersensitivity to dimethyl fumarate or any of the excipients of TECFIDERA. Serious side effects include anaphylaxis and angioedema, and 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, herpes zoster and other serious infections, liver injury and flushing. In clinical trials, the most common adverse events associated with TECFIDERA were flushing, abdominal pain, diarrhea and nausea.

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 Biogen
As pioneers in neuroscience, Biogen discovers, develops, and delivers worldwide innovative therapies for people living with serious neurological 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, Sir Kenneth Murray, and Nobel Prize winners Walter Gilbert and Phillip Sharp. Today, Biogen has a leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for spinal muscular atrophy, and is providing the first and only approved treatment to address a defining pathology of Alzheimer's disease. Biogen is also commercializing biosimilars and focusing on advancing the industry's most diversified pipeline in neuroscience that will transform the standard of care for patients in several areas of high unmet need.

In 2020, Biogen launched a bold 20-year, $250 million initiative to address the deeply interrelated issues of climate, health, and equity. Healthy Climate, Healthy Lives™ aims to eliminate fossil fuels across the company's operations, build collaborations with renowned institutions to advance the science to improve human health outcomes, and support underserved communities.

The company routinely posts information that may be important to investors on our website at www.biogen.com. To learn more, please visit www.biogen.com and follow Biogen 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 TYSABRI and VUMERITY; the results of certain real-world data; clinical trials and data readouts and presentations; the identification and treatment of MS; our research and development program for the treatment of MS; the potential benefits of digital health technologies; and the potential of our commercial business, including TYSABRI and VUMERITY. These forward-looking statements may be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "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. 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; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; third party collaboration risks; and the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, results of operations and financial condition. 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.

References:

1. Lizán L, et al. *Patient Prefer Adherence*. 2014;8:1653-1664.
2. Combined post-marketing data based on prescriptions and clinical trials exposure to TYSABRI as of January 31, 2022.
3. Combined post-marketing data based on prescriptions and clinical trials exposure to VUMERITY as of December 31, 2021
4. Combined post-marketing data based on prescriptions and clinical trials exposure to TECFIDERA as of December 31, 2021.

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