New Data at ECTRIMS 2021 Highlight Biogen's Focus on Patient-Centered Outcomes and Improving the MS Patient Experience

October 13, 2021

- *Full analysis of Phase 3b NOVA study provides insights on efficacy of every six-week dosing with natalizumab as compared to the approved every four-week dosing*
- *Real-world analysis shows significantly lower risk of relapse for patients treated with TYSABRI® compared to Ocrevus® (ocrelizumab)*
- *New data from EVOLVE-MS-2 demonstrate that a favorable gastrointestinal (GI) tolerability profile for VUMERITY® (diroximel fumarate) is achieved and maintained with dose titration*

CAMBRIDGE, Mass., Oct. 13, 2021 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced new data from its industry-leading portfolio of multiple sclerosis (MS) therapies. These data include additional results from the NOVA study on the efficacy of every six-week (Q6W) 300mg natalizumab intravenous (IV) administration, results from a comparative real-world evaluation of TYSABRI® (natalizumab) when compared to Ocrevus®(ocrelizumab), as well as outcomes on GI tolerability, persistence and adherence for VUMERITY® (diroximel fumarate). The studies are being presented at the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) virtual meeting, October 13-15, 2021.

"Our focus on improving the MS patient experience continues to shape research initiatives across Biogen's MS portfolio, as demonstrated by presentations at this year's ECTRIMS meeting," said Maha Radhakrishnan, M.D., Chief Medical Officer at Biogen. "These new data build upon the existing body of real-world safety and efficacy evidence for extended interval dosing with natalizumab[1,2,3] and highlight outcomes that are important to patients, including a reduced risk of relapse with TYSABRI and new data on the ability for patients to achieve and maintain an improved gastrointestinal tolerability profile with VUMERITY."

Additional Secondary Endpoints and Exploratory Outcomes from Full NOVA Study Include Evaluation of NEDA and EDSS With Q6W Natalizumab
New late-breaking data from the Phase 3b NOVA study provide additional insights into the efficacy of every six-week (Q6W) 300mg natalizumab IV administration compared to the approved every four-week (Q4W) dose of TYSABRI (n=499) for relapsing-remitting multiple sclerosis. Topline results from the NOVA study were released in August 2021, showing that every six-week administration provides a high level of efficacy in controlling MS disease activity in patients who switched to Q6W after at least one year of disease stability on the approved Q4W IV dosing schedule. New results of exploratory outcomes and additional secondary endpoints presented at ECTRIMS demonstrate that efficacy is maintained on a Q6W schedule:

- Time to first relapse was similar between the two dosing schedules with the proportion who were relapse-free at 72 weeks at 96.9 percent for Q6W and 97.6 percent for Q4W.
- The proportion of patients free of disability worsening was 90.0 percent in the Q6W arm and 92.0 percent in the Q4W arm.
- Disease activity rates were similar between both groups. The proportion of patients with No Evidence of Disease Activity (NEDA) was 70.0 percent for Q6W and 67.4 percent for Q4W. NEDA was defined as no gadolinium enhancing (Gd+) lesions, no new or newly enlarging T2 hyperintense lesions, no relapse and no 24-week confirmed disability worsening (CDW) at 72 weeks. Patients with one or more missing assessments were counted as having not achieved NEDA.
- The safety findings in the NOVA study were consistent with the known safety profile of IV natalizumab, and the incidence of AEs and SAEs were similar between the two treatment arms. One patient with asymptomatic progressive multifocal leukoencephalopathy (PML) in the Q6W arm was high-risk based on the known risk factors, underscoring the importance of the need for continued PML monitoring and risk factor considerations in patients treated with natalizumab.

"Upon complete evaluation of the NOVA data, the results inclusive of secondary and exploratory outcomes offer a more comprehensive understanding of the six-week dosing regimen of natalizumab and its ability to provide a high level of efficacy in controlling MS disease activity," said John Foley, M.D., Rocky Mountain MS Clinic. "Combined with the improvement in safety demonstrated through analyses of data from the TOUCH Prescribing Program, which has shown that a six-week dosing schedule is associated with an 88 percent reduction in the risk of PML[4], these data on the efficacy of every six-week dosing offer valuable information for clinicians."

The NOVA study was designed to assess the efficacy of Q6W dosing with natalizumab IV administration following analyses from the TOUCH (TYSABRI Outreach: Unified Commitment to Health) Prescribing Program, which showed that extended interval dosing was associated with a significant reduction in the probability of PML.[4] Natalizumab is available commercially under the brand name TYSABRI and the only approved dose is 300mg on a Q4W regimen.

A Real-world Analysis Reports Lower Relapse Risk With TYSABRI Than Ocrevus
A new analysis of relapse-related outcomes and healthcare utilization for MS patients being treated with disease-modifying therapies (DMTs) found that those treated with TYSABRI (n=835) had a lower risk of relapse than those treated with Ocrevus (n=3,497). The retrospective analysis of data from a U.S. claims database from April 2017 to September 2020 found:

- The probability of remaining free of any relapse was significantly higher with TYSABRI than with Ocrevus at 12 and 24 months ($p<0.001$);
- Time to first relapse significantly favored TYSABRI over Ocrevus for any relapse (hazard ratio [HR]=0.70; $p<0.01$) and outpatient relapse (HR=0.71; $p<0.01$);

- Time to hospitalized relapse was numerically better for TYSABRI compared to Ocrevus but did not differ significantly between treatments (HR=0.61; p=0.11);
- There were no significant differences in annualized costs for relapse-related hospital encounters or steroid use observed between the two treatments and time to first MS-related ER visit did not differ significantly between treatments (HR=1.05; p=0.81).

New EVOLVE-MS-2 Study Results Suggest Consistent GI Tolerability for VUMERITY Throughout Dose Titration May Prevent Delays in Reaching Maintenance Dose

In the Phase 3 EVOLVE-MS-2 study, VUMERITY (n=253) demonstrated that an improved GI tolerability profile compared to TECFIDERA® (dimethyl fumarate) (n=251) may simplify initiation of therapy. A new analysis presented at the meeting examines GI tolerability during the dose titration period and during the maintenance dose period over the course of the study for individuals starting therapy on VUMERITY relative to TECFIDERA. In addition to reinforcing VUMERITY's tolerability profile based on less frequent and less severe GI events versus TECFIDERA, key findings include:

- Weekly incidence of GI adverse events (AEs) remained consistent and low throughout the 5-week treatment period for VUMERITY but increased in number and severity for TECFIDERA after titration to the full dose, peaking in Weeks 3 and 4.
- Throughout the 5-week treatment period, moderate/severe GI AEs were less likely with VUMERITY (1.6%–4.8% versus 4.4%–13.9% with TECFIDERA).
- Discontinuations due to GI AEs were 0.8 percent for VUMERITY and 4.8 percent for TECFIDERA; most TECFIDERA discontinuations occurred in Week 3 (58.3 percent)

"These findings suggest GI tolerability is consistent across the doses with VUMERITY, which may enable patients to potentially reach the maintenance dose with less dose interruptions," said Robert Naismith, M.D., of Washington University School of Medicine. "Reducing the need for physicians to utilize real-world GI mitigation strategies has the potential to have a positive impact on treatment compliance and adherence."

Data Presentations Featured at ECTRIMS:

- Primary Results of NOVA: A Randomised Controlled Study of the Efficacy of 6-Week Dosing of Natalizumab Versus Continued 4-Week Treatment for Multiple Sclerosis (P970)
- Claims-based Relapse and Hospitalisation Rates in Patients With Multiple Sclerosis Treated With Natalizumab or Ocrelizumab (P833)
- Comparing the Impact of Dose Titration on Gastrointestinal Tolerability: Diroximel Fumarate Versus Dimethyl Fumarate in Patients With Relapsing-Remitting Multiple Sclerosis (P692)

About TYSABRI® (natalizumab)

TYSABRI is a well-established treatment indicated for relapsing forms of multiple sclerosis (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. 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 a single disease-modifying treatment (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 approved in over 80 countries, and approximately 233,000 people worldwide have been treated with TYSABRI, with over 927,000 patient-years of experience, based on clinical trials and prescription data.[5]

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-JCV 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), and infections including opportunistic infections, and a reduction in blood platelet counts.

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 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 530,000 patients have been treated with it, representing more than 1,000,000 patient-years of exposure across clinical trial use and patients prescribed TECFIDERA.[6]

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
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. Today Biogen has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for spinal muscular atrophy, commercializes biosimilars of advanced biologics and is focused on advancing research programs in multiple sclerosis and neuroimmunology, Alzheimer's disease and dementia, neuromuscular disorders, movement disorders, ophthalmology, neuropsychiatry, immunology, acute neurology and neuropathic pain.

We routinely post information that may be important to investors on our website at www.biogen.com.
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, about the potential benefits, safety and efficacy of TYSABRI (natalizumab), VUMERITY and Q6W; the results of the NOVA Phase 3b study, the results of the EVOLVE-MS-2 study and certain real-world data; clinical trials and data readouts and presentations; and the treatment of MS. 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. 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 uncertainty of success in the development and potential commercialization of Q6W; unexpected concerns that may arise from additional data, analysis or results obtained during the NOVA Phase 3b study, the EVOLVE-MS-2 study or other clinical studies of TYSABRI (natalizumab), VUMERITY and Q6W; the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of expansion of product labeling; 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; 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. Chisari et al. Clinical effectiveness of different natalizumab interval dosing schedules in a large Italian population of patients with multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2020;0:1–7. doi: 10.1136/jnnp-2020-323472.
2. Butzkueven H et al. Similar Clinical Outcomes for Natalizumab Patients Switching to Every-6-Week Dosing Versus Remaining on Every-4-Week Dosing in Real-World Practice. Poster presented at 8th Joint ACTRIMS-ECTRIMS Virtual Meeting; September 11–13, 2020. P0393.
3. Zhovtis Ryerson L et al. No Difference in Radiologic Outcomes for Natalizumab Patients on Extended Interval Dosing Compared with Standard Interval Dosing in MS PATHS. Poster presented at American Academy of Neurology Virtual Annual Meeting; April 17-22,2021. P15.210.
4. Zhovtis Ryerson et al. 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. Poster presented at American Academy of Neurology Virtual Annual Meeting; April 17-22, 2021.P15.201
5. Combined post-marketing data based on prescriptions and clinical trials exposure to TYSABRI as of July 31, 2021.
6. Combined post-marketing data based on prescriptions and clinical trials exposure to TECFIDERA as of June 30, 2021.

MEDIA CONTACT:
Ashleigh Koss
+ 1 908 205 2572
public.affairs@biogen.com

INVESTOR CONTACT:
Mike Hencke
+1 781 464 2442
IR@biogen.com