New Data at ACTRIMS-ECTRIMS Meeting Showcase Safety and Efficacy of Biogen's Industry-Leading MS Portfolio

September 11, 2020

- *New data from ongoing Phase 3 study further define the effectiveness and improved GI tolerability of VUMERITY® (diroximel fumarate)*
- *Real-world findings evaluate quality of life benefits associated with TYSABRI® (natalizumab) when compared to Ocrevus®(ocrelizumab)*
- *Additional real-world findings report positive benefits of PLEGRIDY® (peginterferon beta-1a) and AVONEX® (interferon beta-1a) in older individuals with relapsing multiple sclerosis*

CAMBRIDGE, Mass., Sept. 11, 2020 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced new data underscoring the efficacy and safety of its broad, industry-leading portfolio of multiple sclerosis (MS) therapies. These data will be presented during MSVirtual2020, the eighth joint meeting of the Americas Committee for Treatment and Research in Multiple Sclerosis and the European Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS-ECTRIMS), which will be held virtually September 11-13, 2020.

"We at Biogen are proud of our commitment to addressing both the urgent and long-term challenges facing people living with MS," said Maha Radhakrishnan, M.D., Chief Medical Officer at Biogen. "The data we are presenting at ACTRIMS-ECTRIMS highlight the improved outcomes that our broad MS portfolio has continued to provide for people with relapsing forms of MS, regardless of where they are in their treatment journey, as well as our ongoing investment in research and development to identify potentially effective drug candidates."

New Phase 3 Data Further Characterize the Effectiveness and Patient-Reported GI Tolerability of VUMERITY® (diroximel fumarate)
New data from the VUMERITY Phase 3 clinical program further define the effectiveness and safety profile of Biogen's latest oral fumarate therapy. Findings from the five-week EVOLVE-MS-2 study reinforce clinically meaningful improvements in patient-assessed gastrointestinal (GI) tolerability associated with VUMERITY treatment (n=253) compared to TECFIDERA® (dimethyl fumarate) (n=251), and support its impact on quality of life for people with relapsing MS. Study participants taking VUMERITY reported a lower likelihood of experiencing GI symptoms that interfered with daily activities or were associated with missed work, as well as less concomitant medication use to treat GI symptoms.

An exploratory analysis from the ongoing EVOLVE-MS-1 study assessed the effects of VUMERITY on brain volume change and other clinical measures in people with relapsing MS (n=365) treated for up to two years. Separate studies have shown brain volume loss may be associated with cognitive impairment, physical disability and reduced quality of life in people with MS.[1,2] Data from EVOLVE-MS-1 show:

- The annual rate of brain volume change in study participants treated with VUMERITY for two years was similar to the rate observed in healthy individuals; and
- Approximately 90 percent of people treated with VUMERITY remained free from confirmed disability progression and around 84 percent were relapse-free at two years.

Also being presented at the meeting are final data from the Phase 3 ENDORSE study, which further demonstrate the sustained efficacy and well-characterized safety profile of TECFIDERA in patients followed for up to 13 years.

Real-World Data From Separate Analyses in the Relapsing MS Population Show Improved Outcomes With TYSABRI® (natalizumab), PLEGRIDY® (peginterferon beta-1a) and AVONEX® (interferon beta-1a)
Through MS PATHS (Partners Advancing Technology and Health Solutions), Biogen is collaborating with leading MS centers in Europe and the U.S. to generate standardized, high-quality data from a diverse, real-world MS patient population. To date, more than 17,000 patients have been enrolled in MS PATHS. Data being presented from treatment in the real-world setting support improved outcomes associated with TYSABRI, PLEGRIDY and AVONEX. Results from separate analyses of MS PATHS data reveal the following:

- In the first comparison of MS PATHS standardized magnetic resonance imaging (MRI) protocols, analyses of changes in brain MRI (occurring over a mean follow-up of 0.8 years) were compared during natalizumab treatment with extended interval dosing (EID; n=85) to the approved every-four-week (Q4W; n=569) dosing. The analysis reported no significant differences in the rates of new T2 lesions, T2 lesion volumes and brain atrophy. Differences in MRI scanners and acquisition protocols in clinical practice have made comparisons of brain MRI outcomes challenging. Multiple real-world studies have suggested the effectiveness of natalizumab EID is similar to the approved Q4W dosing.[3-7] Biogen continues to evaluate the efficacy, safety and tolerability of natalizumab EID through the prospective NOVA trial (NCT03689972), and recently filed with regulatory authorities for a subcutaneous dosing formulation which, if approved, would allow for more options for TYSABRI administration.

- Treatment with TYSABRI was associated with greater improvements than Ocrevus® (ocrelizumab) in several quality of life domains according to the Neuro-QoL (Quality of Life in Neurological Disorders) assessment. In a subgroup analysis of matched patients treated with TYSABRI or Ocrevus, significant improvement was observed in nine of 12 Neuro-QoL domains in patients treated with TYSABRI (n=144) and in four of 12 domains in patients treated with Ocrevus (n=502). Overall, annualized rates of improvement were higher with TYSABRI than with Ocrevus and significant differences were observed in three domains: positive affect and well-being, satisfaction with social roles and activities and sleep

disturbance.

- Clinical outcomes in people with MS aged 60 or older (n=286), compared to those under 60 (n=729), indicate that PLEGRIDY and AVONEX may provide real-world treatment benefits over two years in both age groups. Data show functional improvements in processing speed test (PST) and contrast sensitivity test (CST) over one year in both age groups. Additionally, a majority of participants in both age groups remained free from relapse over two years.

Data From a Phase 1 Study of BIIB091 Supports Continued Development for the Treatment of MS
Biogen also presented data from a Phase 1 study of BIIB091, an orally active selective, reversible (noncovalent), small molecule inhibitor of Bruton's Tyrosine Kinase (BTK). Data evaluated the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple ascending oral doses in healthy adult participants. Selective BTK inhibition may be beneficial for the treatment of MS by preventing B-cell and myeloid cell activation without immune cell depletion.

Data Presentations Featured at ACTRIMS-ECTRIMS:
Note: All poster presentations from MSVirtual2020 will be made available online at 8 a.m. ET on Friday, September 11, 2020.

- Improved GI Tolerability With Diroximel Fumarate is Associated With Clinically Meaningful Benefits on Quality of Life Compared With Dimethyl Fumarate in EVOLVE-MS-2 (Poster 0214)
- Effects of Diroximel Fumarate on Brain Volume Change and Disability Progression in Adults With Relapsing-Remitting Multiple Sclerosis From EVOLVE-MS-1 (Poster P0205)
- Safety and Efficacy in Patients Treated With Dimethyl Fumarate and Followed for 13 Years: Final Results of ENDORSE (Platform FC02.05 – Sunday, September 13, 1:48-2:00 p.m. ET)
- No Difference in Radiologic Outcomes for Natalizumab Patients on Extended Interval Dosing Compared With Standard Interval Dosing in MS PATHS (Poster P0360)
- Impact of Natalizumab on Quality of Life in a Real-World Cohort of Patients With Multiple Sclerosis: Results from MS PATHS (Poster P1036)
- Characteristics and Clinical Outcomes of Older Patients With MS Treated With Peginterferon Beta-1a or Intramuscular Interferon Beta-1a in MS PATHS (Poster P0843)
- A Phase 1 Study of BIIB091, a Bruton's Tyrosine Kinase (BTK) Inhibitor, in Healthy Adult Participants: Preliminary Results (Poster P0186)

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 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 475,000 patients have been treated with it, representing more than 950,000 patient-years of exposure across clinical trial use and patients prescribed TECFIDERA. Of these, 6,335 patients (14,241 patient-years) were from clinical trials.[8]

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 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 213,000 people worldwide have been treated with TYSABRI, with over 835,000 patient-years of experience, based on clinical trials and prescription data.[9]

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) 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 PLEGRIDY® (peginterferon beta-1a)
PLEGRIDY is a subcutaneous pegylated interferon dosed once every two weeks for relapsing forms of multiple sclerosis (MS) in adults, the most common form of MS. PLEGRIDY is currently approved in over 60 countries including the U.S., Canada, Australia and Switzerland and across the European Union. Nearly 57,000 people worldwide have been treated with PLEGRIDY, with over 107,000 patient-years of experience, based on prescription data.[10] Biogen continues to work toward making PLEGRIDY available in additional countries across the globe.

The efficacy and safety of PLEGRIDY are supported by one of the largest pivotal studies with interferons conducted in people living with relapsing-remitting MS. In clinical studies, PLEGRIDY has been proven to significantly reduce the rate of MS relapses, slow the progression of disability and reduce the number of MS brain lesions while demonstrating a well-characterized safety profile for patients with relapsing forms of MS. Side effects reported include liver problems, including liver failure and increases in liver enzymes; depression or suicidal thoughts; serious allergic reactions; cardiac problems, including congestive heart failure; autoimmune disorders; decreases in white blood cell or platelet counts; and seizures. In clinical trials, the most common adverse events associated with PLEGRIDY were injection site reactions and flu-like symptoms. A list of adverse events can be found in the full PLEGRIDY product labeling for each country where it is approved.

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

About AVONEX® (interferon beta-1a)
AVONEX is prescribed for relapsing forms of MS and is currently approved in over 90 countries. Over 580,000 people worldwide have been treated with AVONEX, with over 2.6 million patient-years of experience, based on prescription data.[11] AVONEX is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Symptoms of depression, suicidal ideation or psychosis, and cases of suicide, have been reported with increased frequency with patients receiving AVONEX. Severe hepatic injury, including cases of hepatic failure has been reported rarely in patients. Rare cases of anaphylaxis have been reported. While beta interferons do not have any known direct cardiac toxicity, cases of congestive heart failure, cardiomyopathy and cardiomyopathy with congestive heart failure have been reported in patients without known predisposition. Decreased peripheral blood counts have been reported from postmarketing experience. Seizures have been reported in patients using AVONEX, including patients with no prior history of seizure. Autoimmune disorders of multiple target organs have been reported. Routine periodic blood chemistry, hematology, liver function and thyroid function tests are recommended.

Please click here for Important Safety Information and full Prescribing Information, including Medication Guide for AVONEX 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, immunology, neurocognitive disorders, acute neurology and pain.

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 VUMERITY, TECFIDERA, TYSABRI, PLEGRIDY and BIIB091; the results of certain real-world data; results from the EVOLVE-MS-2 study, Phase 3 ENDORSE study and the Phase 1 study of BIIB091; the identification and treatment of MS; our research and development program for the treatment of MS; potential regulatory discussions, submissions and approvals and the timing thereof; the potential of Biogen's commercial business, including VUMERITY, TECFIDERA, TYSABRI, PLEGRIDY and BIIB091; 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," "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 the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis; risks of unexpected costs or delays; unexpected concerns may arise from additional data, analysis or results obtained during clinical trials; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates or expansion of product labeling; failure to obtain regulatory approvals in other jurisdictions; 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. Mowry EM, Beheshtian A, Waubant E, et al. Quality of life in multiple sclerosis is associated with lesion burden and brain volume measures. Neurology. 2009;72(20):1760-1765.
2. Lanz M, Hahn HK, Hildebrandt H. Brain atrophy and cognitive impairment in multiple sclerosis: a review [published correction appears in J Neurol. 2008 Feb;255(2):309-10]. J Neurol. 2007;254 Suppl 2:II43-II48.
3. Foley J, Xiong K, Hoyt T, et al. Serum neurofilament light levels in patients with relapsing-remitting multiple sclerosis switching from natalizumab every-4-week dosing to extended interval dosing. AAN 2020; S10.009.
4. Butzkueven, Kappos L, Spelman T, et al. No significant difference in relapse outcomes in patients switching to natalizumab extended interval dosing or remaining on standard interval dosing: propensity score comparative effectiveness analysis of patients in the TYSABRI Observational Program. ECTRIMS 2019; P1033.
5. Yamout B, Sahraian MA, Ayoubi NE, et al. Efficacy and safety of natalizumab extended interval dosing. *Mult Scler Relat Disord.* 2018;24:113-116.
6. Zhovtis Ryerson L, Frohman TC, Foley J, et al. Extended interval dosing of natalizumab in multiple sclerosis. J Neurol Neurosurg Psychiatry. 2016;87:885-889.
7. Bomprezzi R, Pawate S. Extended interval dosing of natalizumab: a two-center, 7-year experience. Ther Adv Neurol Disord. 2014;7:227-231.
8. Combined post-marketing data based on prescriptions and clinical trials exposure to TECFIDERA as of June 30, 2020.
9. Combined post-marketing data based on prescriptions and clinical trials exposure to TYSABRI as of July 31, 2020.
10. Combined post-marketing data based on prescriptions for PLEGRIDY as of March 31, 2020.
11. Combined post-marketing data based on prescriptions for AVONEX as of March 31, 2020.

MEDIA CONTACT:
David Caouette
+ 1 617 679 4945
public.affairs@biogen.com

INVESTOR CONTACT:
Joe Mara
+1 781 464 2442
IR@biogen.com