Biogen To Present Data At AAN Highlighting Its Innovative Marketed Treatments And Investigational Pipeline Programs For Complex Neurodegenerative Diseases

May 1, 2019

- *Data demonstrate that pre-symptomatic infants with SMA treated with SPINRAZA® (nusinersen) over three years achieved motor milestones that are more consistent with normal childhood development*
- *Late-breaking data expand on safety and exploratory efficacy results of a study investigating tofersen (BIIB067) for the treatment of amyotrophic lateral sclerosis with a confirmed superdioxide dismutate 1 (SOD1) mutation*
- *Data from industry-leading multiple sclerosis (MS) portfolio and pipeline highlight ongoing innovations to meet the diverse needs of people living with MS, including additional pivotal data for diroximel fumarate*

CAMBRIDGE, Mass., May 01, 2019 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced it will present new data across its industry-leading neuroscience portfolio and advancing clinical development programs at the 71st annual meeting of the American Academy of Neurology (AAN) in Philadelphia, PA. (May 4–11). Of Biogen's 33 total presentations, key data will focus on spinal muscular atrophy (SMA), multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS).

"Biogen stands at the forefront of neuroscience, taking on some of the most challenging diseases in history as part of our steadfast commitment to supporting patients with a range of complex and rare neurological disorders," said Alfred Sandrock, Jr., M.D., Ph.D., executive vice president and chief medical officer at Biogen. "Our data at AAN illustrate our drive to advance critical research for people who have limited or no treatment options."

Research across Biogen's clinical and development programs demonstrates the company's commitment to further understanding neurodegenerative diseases with unmet need. SMA and MS data focus on validating biomarkers that aid in monitoring and detecting disease progression, while pipeline data underscore the company's emphasis on thoughtful study design and understanding the patient journey.

SMA Data Presentations Reinforce SPINRAZA as Standard of Care in Treating SMA, Underscoring Therapy's Long-Term Benefit for Infants, Children and Adults

- Results from the NURTURE study demonstrate that pre-symptomatic infants with SMA treated with SPINRAZA over three years achieved motor milestones more consistent with normal childhood development.
- After three years of follow-up, interim results from the ENDEAR/CHERISH/SHINE open-label extension study show that treatment with SPINRAZA, particularly when initiated earlier, leads to progressive motor milestone improvements and increased survival rates for individuals with infantile-onset SMA.
- Additional data suggest that phosphorylated neurofilament heavy chain (pNF-H) may emerge as a promising biomarker to predict disease activity in SMA.

Advancing Biogen's Pipeline of Investigational Treatments for Neurodegenerative Diseases

- In a late-breaking presentation, Biogen will share expanded findings from its phase 1/2 study of tofersen (BIIB067) for the investigational treatment of ALS with a confirmed SOD1 mutation. Positive interim results of the study, as well as Biogen's decision to exercise its option to obtain a license from Ionis Pharmaceuticals Inc. to develop and commercialize the asset, were announced in December 2018. Biogen has advanced the program to the ongoing phase 3 clinical study (VALOR), which is a continuation of the Phase 1/2 study. Biogen is collaborating with regulators to further define the scope of the clinical data package required to support the registration of BIIB067.
- Other pipeline data to be presented advance the scientific community's understanding of rare neurodegenerative diseases, including progressive supranuclear palsy (PSP), and provide updates on Biogen's investigational programs for stroke and neuropathic pain.

Advancing Biogen's Portfolio of Leading MS Therapies

- Safety and exploratory efficacy results from the ongoing pivotal EVOLVE-MS-1 study with diroximel fumarate (BIIB098) will be shared, which support the potential of Biogen and Alkermes' investigational oral treatment as a new option for patients with relapsing MS. 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 improving patient care and further understanding the benefit-risk profile of TYSABRI® (natalizumab), Biogen will present updated safety analyses evaluating extended interval dosing of natalizumab (of approximately every 6 weeks) compared to every 4-week dosing.
- Biogen continues to engage in collaborative research efforts to identify potential biomarkers in MS, and will present results further confirming serum neurofilament light (sNfL) as a clinically useful tool for disease prognosis and treatment management.

Highlights of Biogen's Platform and Poster Presentations:

SPINAL MUSCULAR ATROPHY

Platform Presentations

- Nusinersen in Infants Who Initiate Treatment in a Presymptomatic Stage of Spinal Muscular Atrophy (SMA): Interim Efficacy and Safety Results From the Phase 2 NURTURE Study – *Platform S25.001 – Tuesday, May 7, 1:00 p.m. ET*
- Interim Report on the Safety and Efficacy of Longer-Term Treatment With Nusinersen in Infantile-Onset Spinal Muscular Atrophy (SMA): Updated Results From the SHINE Study – *Platform S25.004 – Tuesday, May 7, 1:33 p.m. ET*
- Association of Phosphorylated Neurofilament Heavy Chain (pNF-H) Levels With Motor Function Achievement in Individuals With Spinal Muscular Atrophy (SMA) Treated With Nusinersen – *Platform S27.009 – Tuesday, May 7, 2:28 p.m. ET*

Poster Presentations

- Symptoms and Complications Over Three Years Among Later Childhood, Adolescent and Adult Spinal Muscular Atrophy Patients: A Natural History Study Within U.S. Hospitals – *Poster P1.6-051 – Sunday, May 5, 11:30 a.m. – 6:30 p.m. ET*
- Ambulation Status, Role Participation and Caregiver Assistance Among Individuals With Spinal Muscular Atrophy Type III: Results from the Cure SMA Membership Survey – *Poster P1.6-061 – Sunday, May 5, 11:30 a.m. – 6:30 p.m. ET*
- Interim Report on the Safety and Efficacy of Longer-Term Treatment With Nusinersen in Later-onset Spinal Muscular Atrophy (SMA): Results from the SHINE Study – *Poster P1.6-063 – Sunday, May 5, 11:30 a.m. – 6:30 p.m. ET*

PIPELINE
Emerging Science (Late Breaking) Presentation

- Safety, PK, PD, and Exploratory Efficacy in Single and Multiple Dose Study of a SOD1 Antisense Oligonucleotide (BIIB067) Administered to Participants With ALS – *Poster 007 – Tuesday, May 7, 11:45 a.m. – 12:45 p.m. ET*

Poster Presentations

- CONVEY, A Phase 2 Placebo-Controlled, Double-Blind, Enriched Enrollment Randomized Withdrawal Study Design of Vixotrigine for the Treatment of Pain in Participants With Confirmed Small Fiber Neuropathy – *Poster P2.6-068 – Monday, May 6, 11:30 a.m. – 6:30 p.m. ET*
- Design of a Phase III Study of Intravenous Glibenclamide (BIIB093) for Large Hemispheric Infarction: the CHARM Study – *Poster P2.3-036 – Monday, May 6, 11:30 a.m. – 6:30 p.m. ET*
- The Diagnostic Journey of Patients With Progressive Supranuclear Palsy (PSP) in US Electronic Medical Record Data – *Poster P3.8-007 – Tuesday, May 7, 11:30 a.m. – 6:30 p.m. ET*
- Incidence of Venous Thromboembolic Events Among Amyotrophic Lateral Sclerosis in a US Health Insurance Claims Database – *Poster P4.6-003 – Wednesday, May 8, 11:30 a.m. – 6:30 p.m. ET*

MULTIPLE SCLEROSIS
Platform Presentations

- Natalizumab Reduces Serum Concentrations of Neurofilament Light Chain in Secondary Progressive Multiple Sclerosis Patients From the Phase 3 ASCEND Study – *Platform S12.008 – Monday, May 6, 1:00 – 3:00 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, 1:00 – 3:00 p.m. ET*
- 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 – 3:00 p.m. ET*
- Pregnancy and Infant Outcomes With Interferon Beta: Data From the European Interferon Beta Pregnancy Registry and MS Preg Study Conducted in Finland and Sweden – *Platform S49.005 – Thursday, May 9, 1:00 – 3:00 p.m. ET*

Poster Presentations

- Dimethyl Fumarate Exerts Selective Effects on Key B Cell Subsets and IgG Levels Which May Contribute to Its Therapeutic Benefit in MS While Maintaining Protective Humoral Immunity – *Poster P.2.2-069 – Monday, May 6, 11:30 a.m. – 6:30 p.m. ET*
- 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*
- Longitudinal Stability of Anti–JC Virus (JCV) Antibody Index Over 2 Years in Multiple Sclerosis (MS) Patients Treated With Natalizumab in the ASCEND Study – *Poster P4.2-009 – Wednesday, May 8 11:30 a.m. – 6:30 p.m. ET*
- Delayed-release Dimethyl Fumarate Treatment Shifts the Immune Repertoire in Patients With Relapsing-Remitting Multiple Sclerosis: Results of PROCLAIM, an Open-label Phase 3 Study – *Poster P4.2-053 – Wednesday, May 8 11:30 a.m. – 6:30 p.m. ET*

About SPINRAZA® (nusinersen)[1-4]
SPINRAZA is the first and only approved medicine for the treatment of spinal muscular atrophy (SMA) and is currently available in more than 40 countries. As of March 31, 2019 over 7,500 individuals with SMA are being treated with SPINRAZA worldwide, based on patients across the post-marketing setting, Expanded Access Program (EAP) and clinical trial participants.

SPINRAZA is an antisense oligonucleotide (ASO) developed using Ionis' proprietary antisense technology that is designed to treat the root cause of SMA. SPINRAZA alters the splicing of SMN2 pre-mRNA in order to increase production of full-length SMN protein. ASOs are short synthetic strings of nucleotides designed to selectively bind to target RNA and regulate gene expression. Through use of this technology, SPINRAZA has been shown to increase the amount of full-length SMN protein in individuals with SMA. SPINRAZA is administered via intrathecal injection, which delivers therapies directly into the cerebrospinal fluid (CSF) around the spinal cord, where motor neurons degenerate in individuals with SMA due to insufficient levels of SMN protein.

In the clinical trial program, SPINRAZA demonstrated a favorable benefit-risk profile. The most common adverse reactions that occurred in the SPINRAZA group were respiratory infection and constipation. Serious adverse reactions of atelectasis were more frequent in SPINRAZA-treated patients. Coagulation abnormalities and thrombocytopenia, including acute severe thrombocytopenia, have been observed after administration of some ASOs. Individuals may be at increased risk of bleeding complications. Renal toxicity has been observed after administration of some ASOs. SPINRAZA is present in and excreted by the kidney.

Biogen licensed the global rights to develop, manufacture and commercialize SPINRAZA from Ionis Pharmaceuticals, Inc. (Nasdaq: IONS), a leader in antisense therapeutics. Biogen and Ionis conducted an innovative clinical development program, the largest of its kind in SMA, that moved SPINRAZA from its first dose in humans in 2011 to its first regulatory approval in five years.

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.[5] 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 Tofersen
Tofersen is an antisense oligonucleotide (ASO) RNase H-mediated inhibitor of SOD1 messenger ribonucleic acid (mRNA) being developed for the treatment of ALS with SOD1 mutations. Tofersen binds to SOD1 mRNA, allowing its degradation by RNase-H and reducing protein production. This is thought to decrease the toxicity of mutant SOD1 and potentially provide therapeutic benefit through improved survival and function to people with ALS with SOD1 mutations. Tofersen demonstrated proof-of-biology and proof-of-concept in a Phase 1 analysis. Biogen licensed tofersen from Ionis Pharmaceuticals, Inc. under a collaborative development and license agreement.

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, about the potential benefits, safety and efficacy of SPINRAZA, TYSABRI, diroximel fumarate and tofersen; the results of certain real-world data; clinical trial results and plans; our research and development program for the treatment of SMA, MS and ALS and clinical studies on MS, ALS, PSP, stroke and neuropathic pain; the identification and treatment of SMA and MS; risks and uncertainties associated with drug development and commercialization; potential regulatory approval and the timing thereof; the potential of Biogen's commercial business and pipeline programs, including SPINRAZA, TYSABRI, diroximel fumarate and tofersen; and the anticipated benefits and potential of Biogen's collaboration arrangements with Ionis and Alkermes;. These 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 or results

obtained during our clinicial 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; regulatory submissions may take longer or be more difficult to complete than expected; uncertainty of success in the development and potential commercialization of VUMERITY and tofersen; 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; 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; the risk that we may not fully enroll our clinical trials or enrollment will take longer than expected; 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 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:

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