Biogen Builds on Its 40-Year Legacy in Neuroscience with Presentation of Research from Its Portfolio of Medicines and Investigational Programs for Neurodegenerative Diseases

April 17, 2018

- *New data underscore benefits of SPINRAZA® (nusinersen) across broad spinal muscular atrophy (SMA) populations and include longer-term efficacy and safety assessments from the SHINE study*
- *Data from Biogen's multiple sclerosis (MS) research programs include results from clinical investigation of a potential biomarker for MS and new insights from MS PATHS, its Learning Health System, which may inform future care approaches*
- *Data from movement disorder programs support further clinical development of Biogen's investigational compounds forParkinson's disease and progressive supranuclear palsy*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 17, 2018-- Biogen (Nasdaq: BIIB) announced it will present data from its portfolio of marketed treatments and clinical development programs for some of the most complex and difficult-to-treat neurodegenerative diseases at the 70th annual meeting of the American Academy of Neurology (AAN) in Los Angeles (April 21–27).

"Biogen's research efforts are focused on helping to improve the lives of the approximately one billion people affected by neurological disorders, [1]" said Alfred Sandrock, Jr., M.D., Ph.D., executive vice president and chief medical officer at Biogen. "The data we are presenting at AAN reflect the work we are conducting on multiple fronts, including research to better understand challenging nervous system diseases and the clinical development of investigational treatments for what we believe are some of the most significant unmet medical needs."

Platform and poster presentations will highlight the benefits SPINRAZA (nusinersen) provides for individuals with spinal muscular atrophy (SMA) across the age and disease spectrum; the company's multiple sclerosis (MS) therapies and non-therapeutic research collaborations designed to elevate the care of MS; and the company's investigational therapies for Alzheimer's disease, Parkinson's disease (PD) and progressive supranuclear palsy (PSP).

Building on Substantial Data, Long-Term Benefits for Broad SMA Populations

- Biogen will present data demonstrating that with SPINRAZA treatment, older patients were able to walk longer distances while experiencing stable or less fatigue at the same time, in contrast to SMA natural history data. The study participants had Type 2 or 3 SMA and were ages 2-15 years at study enrollment.
- Several other analyses illustrating SPINRAZA's effectiveness will be presented, including part one of the Phase 2 EMBRACE study as well as an interim analysis of the SHINE open-label extension study. Featured in AAN's Emerging Science program, the SHINE analysis examined the longer-term safety and efficacy of SPINRAZA in infantile-onset SMA patients.

Elevating the Care of MS

- Data from Biogen's collaborative research initiative to identify a quantitative blood biomarker of MS disease severity will be presented. These data further support serum neurofilament light (NfL) as a promising biomarker for disease severity stratification and treatment monitoring in MS. A biomarker like NfL levels may enhance treatment decision-making and ultimately lead to better long-term outcomes for people with MS.
- Biogen will present updates from MS PATHS (Multiple Sclerosis Partners Advancing Technology and Health Solutions), a collaboration with 10 leading MS centers in the U.S. and Europe that leverages technology deployed in routine care to generate standardized, high-quality data. Researchers anticipate more than 15,000 people with MS will participate in the study. MS PATHS allows researchers to evaluate common and disruptive MS symptoms, such as cognitive changes, to help drive more evidence-based, personalized treatment decisions.
- Real-world data will be presented that demonstrate people with relapsing MS treated with TECFIDERA® (dimethyl fumarate) or TYSABRI® (natalizumab) early in the course of their disease may experience better long-term outcomes.
- MRI and relapse results from the Phase 3 EVOLVE-MS-1 study for BIIB098 (formerly known as ALKS 8700) in patients with relapsing remitting MS will be featured in AAN's Emerging Science program. BIIB098 is an oral, monomethyl fumarate (MMF) prodrug in Phase 3 development for the treatment of relapsing forms of MS.

Advancing the Company's Neurodegenerative Pipeline

- Data from the Phase 1b study of aducanumab, Biogen's investigational treatment for the early stages of Alzheimer's disease, will be presented. The aducanumab 36-month data from the Phase 1b PRIME study have been identified by AAN as a 2018 Abstract of Distinction, a program recognizing top scientific achievements in each abstract topic area; 24-month titration data will also be presented.

Both slide presentations will be available concurrently with the applicable session on the Investor section of the Biogen company website, www.Biogen.com.

Aducanumab is currently being evaluated in two global Phase 3 studies, ENGAGE and EMERGE, which are designed to evaluate its safety and efficacy in slowing cognitive and functional impairment in people with mild cognitive impairment (MCI) due to Alzheimer's disease and mild Alzheimer's disease dementia. Aducanumab is thought to target aggregated forms of beta amyloid, including soluble oligomers and insoluble fibrils, which can form into amyloid plaque in the brain of Alzheimer's disease patients. As of October 22, 2017, Biogen and Eisai Co. Ltd. are collaborating on the development and commercialization of aducanumab globally.

- Data from movement disorder programs will be presented at the meeting, including Phase 1 study results for BIIB092 (formerly BMS-986168), the tau-targeting antibody and investigational compound for PSP, as well as details about the design of the ongoing Phase 2 PASSPORT study. PSP is a rare neurodegenerative disease, considered to be a primary tauopathy, characterized by rapidly progressing physical impairments, such as difficulty speaking, swallowing and walking, as well as cognitive/behavioral impairments, such as apathy and dementia. Data for Biogen's investigation compound for PD, BIIB054, an alpha-synuclein targeting antibody, include Phase 1 study results demonstrating a favorable pharmacokinetics, as well as a safety and tolerability profile which support further clinical development.

Highlights of Biogen's platform and poster presentations:

SPINAL MUSCULAR ATROPHY
Platform Presentation

- Longer-term Assessment of the Safety and Efficacy of Nusinersen for the Treatment of Infantile-onset Spinal Muscular Atrophy (SMA): An Interim Analysis of the SHINE Study – *Platform 003 – Tuesday, April 24, 5:51-5:54 p.m. PT*

Posters

- Evaluating Ambulatory Function and Fatigability in Children Treated with Nusinersen – *Poster P2.322 – Monday, April 23, 11:30 a.m.-7:00 p.m. PT*
- Safety and Efficacy of Nusinersen in Infants/Children with Spinal Muscular Atrophy (SMA): Part 1 of the Phase 2 EMBRACE Study – *Poster P2.324 – Monday, April 23, 11:30 a.m.-7:00 p.m. PT*
- Characterization of Later Childhood/Adult Spinal Muscle Atrophy Patients and Their Transitions of Care Within U.S. Hospitals – *Poster P4.454 – Wednesday, April 25, 11:30 a.m.-7:00 p.m. PT*

MULTIPLE SCLEROSIS
Platform Presentations

- Serum Neurofilament Light (NfL): Towards a Blood Test for Prognosis and Disease/Treatment Monitoring in Multiple Sclerosis Patients – *Platform S24.003 – Tuesday, April 24, 3:54-4:06 p.m. PT*
- MRI and Relapse Results for ALKS 8700 in Patients with Relapsing Remitting Multiple Sclerosis: 1-year Interim Results from the Phase 3 EVOLVE-MS-1 Study – *Platform 006 – Tuesday, April 24, 5:45-7:00 p.m. PT*
- Benchmarks of Cognitive Performance in a Large, Representative Patient Population – *Platform S44.007 – Thursday, April 26, 4:42-4:54 p.m. PT*

Posters

- Comparative Effectiveness of Dimethyl Fumarate Versus Fingolimod and Teriflunomide on the Risk of Relapse in MS Patients Switching from First-generation Platform Therapies in the US – *Poster P1.374 – Sunday, April 22, 11:30 a.m.-5:30 p.m. PT*
- A Comparative Effectiveness Analysis Applying a 3-Way Propensity Score Matching to Real-world Data from the MSBase Registry in Preparation for a Cost-effectiveness Model: Patients Switching Within First-line Agents or to Either Natalizumab or Fingolimod in Active Relapsing-remitting Multiple Sclerosis (RRMS) – *Poster P1.369 – Sunday, April 22, 11:30 a.m.-5:30 p.m. PT*
- A Cost-effectiveness Analysis Using Real-world Data from the MSBase Registry: Comparing Natalizumab to Fingolimod in Patients with Inadequate Response to Disease-modifying Therapies in Relapsing-remitting Multiple Sclerosis (RRMS) in Scotland – *Poster P1.364 – Sunday, April 22, 11:30 a.m.-5:30 p.m. PT*
- Comparison of Techniques for Measurement of Brain Volume in Multiple Sclerosis Patients – *Poster P3.354 – Tuesday, April 24, 11:30 a.m.-7:00 p.m. PT*
- The Functional Brain Network Remains Stable in Natalizumab-treated Multiple Sclerosis Patients: A One Year Study – *Poster P3.369 – Tuesday, April 24, 11:30 a.m.-7:00 p.m. PT*
- The Multiple Sclerosis Partners Advancing Technology and Health Solutions (MS PATHS) Patient Cohort – *Poster P4.381*

– *Wednesday, April 25, 11:30 a.m.-7:00 p.m. PT*

- Natalizumab Extended Interval Dosing (EID) is Associated with a Significant Reduction in Progressive Multifocal Leukoencephalopathy (PML) Risk Compared with Standard Interval Dosing (SID) in the TOUCH® Prescribing Program – *Poster P4.475 – Wednesday, April 25, 11:30 a.m.-7:00 p.m. PT*
- Clinical Trial and Post-Marketing Reports Indicate No Increased Risk of Herpes Zoster in Patients Treated with Delayed-release Dimethyl Fumarate – *Poster P5.362 – Thursday, April 26, 11:30 a.m.-7:00 p.m. PT*
- Real-world Strategies for Management of Gastrointestinal Events in Patients Treated with Delayed-release Dimethyl Fumarate: EFFECT Gastrointestinal Sub-study Results – *Poster P5.345 – Thursday, April 26, 11:30 a.m.-7:00 p.m. PT*
- Longer Duration of Natalizumab Exposure May Lessen Return of Disease Activity Following a Switch from Natalizumab to an Oral Therapy: Modelling Real-world Data from Relapsing-remitting Multiple Sclerosis (RRMS) Patients in the TYSABRI® Observational Program (TOP) – *Poster P6.379 – Friday, April 27, 11:30 a.m.-5:30 p.m. PT*
- Real-world Improvement Across Functional Systems (FS) in Relapsing-remitting Multiple Sclerosis (RRMS) Patients Treated with Natalizumab in the TYSABRI Observational Program (TOP) – *Poster P6.383 – Friday, April 27, 11:30 a.m.-5:30 p.m. PT*

PIPELINE
Platform Presentations

- Aducanumab Titration Dosing Regimen: 24-Month Analysis from PRIME, a Randomized, Double-Blind, Placebo-Controlled Phase 1b Study in Patients with Prodromal or Mild Alzheimer's Disease – *Platform S2.003 – Sunday, April 22, 1:24-1:36 p.m. PT*
- Aducanumab 36-Month Data from PRIME: A Randomized, Double-blind, Placebo-controlled Phase 1b Study in Patients with Prodromal or Mild Alzheimer's Disease – *Platform S2.004 – Sunday, April 22, 1:36-1:48 p.m. PT*
- Randomized, Double-blind, Placebo-controlled, Single Ascending Dose Study of Anti-alpha-synuclein Antibody BIIB054 in Patients with Parkinson's Disease – *Platform S26.001 – Tuesday, April 24, 3:30-3:42 p.m. PT*
- Multiple Ascending Dose Study of the Tau-directed Monoclonal Antibody BMS-986168 in Patients with Progressive Supranuclear Palsy – *Platform S27.004 – Wednesday, April 25, 8:24-8:32 a.m. PT*

Poster

- Efficacy and Safety of BIIB092 in Patients with Progressive Supranuclear Palsy: PASSPORT Phase 2 Study Design – *Poster P6.073 – Friday, April 27, 11:30 a.m.-5:30 p.m. PT*

About SPINRAZA®
SPINRAZA is being developed globally for the treatment of SMA.

SPINRAZA is an antisense oligonucleotide (ASO), using Ionis Pharmaceutical Inc.'s proprietary antisense technology, that is designed to treat SMA caused by mutations or deletions in the SMN1 gene located in chromosome 5q that leads to SMN protein deficiency. SPINRAZA alters the splicing of SMN2 pre-mRNA in order to increase production of full-length SMN protein.[2] 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 the potential to increase the amount of full-length SMN protein in individuals with SMA.

SPINRAZA must be administered via intrathecal injection, which delivers therapies directly to the cerebrospinal fluid (CSF) around the spinal cord,[3] where motor neurons degenerate in individuals with SMA due to insufficient levels of SMN protein.[4]

SPINRAZA demonstrated a favorable benefit-risk profile. The most common adverse reactions reported for SPINRAZA were upper respiratory infection, lower 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.

For additional important safety information, and the United States full prescribing information, please visit www.spinraza.com or your respective country's website.

About TECFIDERA®
TECFIDERA is an oral therapy for relapsing forms of MS, including relapsing-remitting MS, the most common form of MS. More than 310,000 patients have been treated with TECFIDERA worldwide with over 540,000 patient-years of experience.[5] 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.[6] 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.

For additional important safety information, and the United States full prescribing information, please visit www.tecfidera.com or your respective country's website.

About TYSABRI®
TYSABRI is a disease modifying therapy (DMT) approved in more than 80 countries including the United States, the European Union, Canada, Australia and Switzerland. In the United States, 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 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 180,000 people treated worldwide and over 635,000 patient-years of experience.[7]

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 was 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 postmarketing 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.

The overall benefit-risk profile of TYSABRI remains positive. For additional important safety information and the full United States prescribing information which includes a full list of adverse events, please visit www.tysabri.com or your respective country's 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 made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 about additional results from the Phase 2 EMBRACE study, Phase 2 SHINE study, and CS2/CS12 study of SPINRAZA, the Phase 3 EVOLVE MS-1 study of BIIB098, the Phase 1b study of aducanumab, the Phase 1 study of BIIB092, and/or the Phase 1 study of BIIB054, the potential clinical effects of SPINRAZA, TECFIDERA, TYSABRI, BIIB098, aducanumab, BIIB092 and/or BIIB054, the identification and treatment of MS and Alzheimer's disease, the treatment of SMA, and clinical studies on Parkinson's disease and PSP. These statements may be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "possible," "potential," "will," and other words and terms of similar meaning, and are based on our current beliefs and expectations. You should not place undue reliance on these statements or the scientific data presented. 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.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation, the risk that we may not fully enroll our clinical trials or enrollment will take longer than expected, unexpected concerns 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, the occurrence of adverse safety events, or we may encounter other unexpected hurdles. 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 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 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.

[1]World Health Organization. Neurological disorders: Public health challenges. 2007. Available at: http://www.who.int/mental_health/neurology/chapter_4_neuro_disorders_public_h_challenges.pdf?ua=1.

[2] Hua Y, Sahashi K, Hung G, Rigo F, Passini MA, Bennett CF, Krainer AR. Antisense correction of SMN2 splicing in the CNS rescues necrosis in a type III SMA mouse model. Genes Dev. 2010 Aug 1; 24(15):16344-44.

[3] Evers MM, Toonen LJ, van Roon-Mom WM. Antisense oligonucleotides in therapy for neurodegenerative disorders. Adv Drug Deliv Rev. 2015;87:90-103.

[4] Lunn MR, Wang CH. Spinal muscular atrophy. Lancet. 2008;371(9630):2120-2133.

[5] Combined post-marketing and clinical trials exposure to TECFIDERA as of 31 January 2018.

[6] TECFIDERA is approved in the European Union for relapsing-remitting multiple sclerosis.

[7] Global Natalizumab (TYSABRI) Postmarketing PML Update, March 2018.

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