



Biogen Highlights Advances from Its Neurology Research Programs and Portfolio of Innovative Medicines at AAN Congress

April 18, 2017

TECFIDERA[®] and TYSABRI[®] Data Support Early Treatment to Improve MS Patient Outcomes

New SPINRAZA[®] Data Show Robust Efficacy and Safety Across a Broad Range of Individuals with SMA

CAMBRIDGE, Mass.--(BUSINESS WIRE)--[Biogen](#) (NASDAQ: BIIB) will present data from its portfolio of treatments and investigational therapies for people with serious neurological and neurodegenerative diseases at the 69th annual meeting of the American Academy of Neurology (AAN) in Boston (April 22-28, 2017). Platform and poster presentations throughout the meeting will highlight Biogen research, including:

- New real-world evidence supporting TECFIDERA[®] (dimethyl fumarate), the world's most prescribed oral medicine for multiple sclerosis (MS), and TYSABRI[®] (natalizumab), the only high-efficacy treatment with more than 10 years of clinical experience, which underscore the importance of early treatment for MS;
- New data further demonstrating the clinically meaningful efficacy and favorable safety of SPINRAZA[®] (nusinersen), the first and only U.S. Food and Drug Administration (FDA)-approved treatment for spinal muscular atrophy (SMA) in pediatric and adult patients;
- Results from the Phase 1b study of aducanumab, an investigational treatment for early Alzheimer's disease, previously presented in December 2016.

"Biogen's commitment to improving outcomes for people living with MS spans more than two decades, during which time we've fundamentally changed the treatment of the disease. We are now applying our expertise in neurology to discover and develop new therapies to address some of the most challenging and complex diseases of the brain," said Alfred Sandrock, executive vice president and chief medical officer at Biogen. "The data from our MS, SMA and Alzheimer's disease programs reflect our desire to advance the understanding of these diseases and make a meaningful difference in the lives of patients."

Multiple Sclerosis Data Reinforce Benefits of Early, Effective Treatment

Biogen offers one of the most robust portfolios of MS medicines in the industry, with therapies to help manage relapsing MS at every stage of the disease. New real-world data comparing TECFIDERA to other oral MS therapies contribute to the body of evidence that TECFIDERA has strong and sustained efficacy in patients early in the course of the disease, such as in those who are newly diagnosed or were previously treated with another disease modifying therapy. Data to be presented at the meeting also support the early and continued use of TYSABRI in appropriate patients with high disease activity.

New SPINRAZA Data Show Robust Efficacy and Safety Across Broad Spectrum of Individuals with SMA

Biogen will present multiple studies evaluating the safety and efficacy of SPINRAZA across individuals who are most likely to develop SMA Types 1, 2 and 3. The results contrast with the natural history of SMA, where individuals experience a progressive decline in motor function and a failure to achieve motor milestones after symptom onset. New end-of-study CHERISH data in individuals with later-onset SMA (most likely to develop SMA Type 2 or Type 3) will be presented during the Emerging Science Platform session. In addition, new interim data from the NURTURE study will assess the efficacy and safety of SPINRAZA initiated in pre-symptomatic infants genetically diagnosed with SMA and the potential benefit of early treatment initiation.

Data from Phase 1b Study of Aducanumab in Early Alzheimer's Disease

Data from a Phase 1b study of aducanumab, Biogen's investigational treatment for early Alzheimer's disease, will be presented at AAN. These data were previously presented at the Clinical Trials on Alzheimer's Disease meeting in December 2016. 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 early Alzheimer's disease. 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. For more information about the Phase 3 studies, including information about participating centers, visit www.ClinicalTrials.gov (NCT02477800 or NCT02484547).

About Biogen

Through cutting-edge science and medicine, Biogen discovers, develops and delivers innovative therapies worldwide for people living with serious neurological and neurodegenerative diseases. Founded in 1978, Biogen is a pioneer in biotechnology and today the Company has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first and only approved treatment for spinal muscular atrophy, and is at the forefront of neurology research for conditions including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis. Biogen also manufactures and commercializes biosimilars of advanced biologics. For more information, please visit www.biogen.com. Follow us on social media – [Twitter](#), [LinkedIn](#), [Facebook](#), [YouTube](#).

About TECFIDERA[®]

TECFIDERA is an oral therapy for relapsing forms of MS, including relapsing-remitting MS, the most common form of MS. More than 240,000 patients have been treated with TECFIDERA worldwide.¹

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.² 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 multiple sclerosis (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 10 years of experience in treating RRMS, and more than 167,000 people treated worldwide and 559,000 patient-years of experience.³

TYSABRI is a monoclonal antibody that selectively binds to $\alpha 4$ -integrin and is thought to interrupt the activity of inflammatory cells in MS patients by blocking the interaction between $\alpha 4\beta 1$ -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 SPINRAZA[®] (nusinersen)

SPINRAZA is being developed globally for the treatment of SMA. SPINRAZA was first approved by the FDA on December 23, 2016 within three months of regulatory filing. Biogen has also submitted regulatory filings in Japan, Canada, Australia and Switzerland and plans to initiate additional filings in other countries in 2017.

SPINRAZA is an antisense oligonucleotide (ASO) that is designed to treat SMA caused by mutations in the chromosome 5q that leads to survival motor neuron (SMN) protein deficiency. SPINRAZA alters the splicing of SMN2 pre-mRNA in order to increase production of full-length SMN protein.⁴ 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 patients with SMA.

SPINRAZA is administered via intrathecal injection, which delivers therapies directly to the cerebrospinal fluid (CSF) around the spinal cord,⁵ where motor neurons degenerate in patients with SMA due to insufficient levels of SMN protein.⁶

The most common adverse reactions reported for SPINRAZA were lower respiratory infection, upper 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 antisense oligonucleotides. Individuals may be at increased risk of bleeding complications. Renal toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. SPINRAZA is present in and excreted by the kidney.

For complete SPINRAZA United States prescribing information please visit www.SPINRAZA.com.

About Aducanumab

Aducanumab (BIIB037) is an investigational compound being developed for the treatment of early Alzheimer's disease. Aducanumab is a human recombinant monoclonal antibody (mAb) derived from a de-identified library of B cells collected from healthy elderly subjects with no signs of cognitive impairment or cognitively impaired elderly subjects with unusually slow cognitive decline using Neurimmune's technology platform called Reverse Translational Medicine (RTM). Biogen licensed aducanumab from Neurimmune under a collaborative development and license agreement.

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. Based on pre-clinical and Phase 1b data to date, aducanumab has been shown to reduce amyloid plaque levels.

In August 2016 aducanumab was accepted into the European Medicines Agency's PRIME program. In September 2016 the FDA accepted aducanumab into its Fast Track program.

Biogen Safe Harbor

This press release contains forward-looking statements, including statements relating to the potential benefits, safety and efficacy of TECFIDERA, TYSABRI, SPINRAZA and aducanumab, the potential impact of our programs, results of certain clinical studies and real-world data. These statements may be identified by words such as "believe," "expect," "may," "plan," "potential," "will" and similar expressions, 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. Factors which could cause actual results to differ materially from our current expectations include 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 or analysis, including data, analysis or results obtained during our clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates, or we may encounter other unexpected hurdles which may be impacted by, among other things, the occurrence of adverse safety events, failure to obtain regulatory approvals in certain jurisdictions, failure to protect intellectual property and other proprietary rights, product liability claims, third party collaboration risks, and the other risks and uncertainties that are described in the Risk Factors section of Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission. Any forward-looking statements speak only as of the date of this press release, and we assume no obligation to update any forward-looking statement.

¹ Combined post-marketing and clinical trials exposure to TECFIDERA as of 31 January 2017.

² TECFIDERA is approved in the European Union for relapsing-remitting multiple sclerosis.

³ As of 28 February 2017.

⁴ 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.

⁵ Evers MM, Toonen LJ, van Roon-Mom WM. Antisense oligonucleotides in therapy for neurodegenerative disorders. *Adv Drug Deliv Rev.* 2015;87:90-103.

⁶ Lunn MR, Wang CH. Spinal muscular atrophy. *Lancet.* 2008;371(9630):2120-2133.

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