Data Presented at AAN Highlight Impact of ZINBRYTA™ (Daclizumab HYP) on Cognitive Outcomes and the Reversibility of Its Targeted Mechanism of Action

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CAMBRIDGE, Mass. & NORTH CHICAGO, Ill.--(BUSINESS WIRE)--New data presented today show that investigational therapy ZINBRYTA™ (daclizumab HYP) provided improvements on cognitive outcome measures in people living with relapsing forms of multiple sclerosis (RMS). Additional data offer insight into ZINBRYTA's targeted mechanism of action (MOA), demonstrating that it did not cause broad immune cell depletion and its effects on total lymphocyte counts were reversible within approximately 8 to 12 weeks upon treatment discontinuation. These results were presented by Biogen (NASDAQ: BIIB) and AbbVie (NYSE: ABBV) at the 68th annual meeting of the American Academy of Neurology (AAN) in Vancouver, Canada.

"We are pleased to present additional analyses from the ZINBRYTA clinical program. This work provides important insights into the immunology behind ZINBRYTA," said Michael Severino, M.D., executive vice president, research and development and chief scientific officer, AbbVie. "We are very encouraged by the results we have seen from ZINBRYTA and are focused on bringing a potential new treatment option to patients who suffer from this devastating disease."

New Analysis Highlights Impact of ZINBRYTA on Cognitive Outcomes for Up to Three Years

A post-hoc analysis of exploratory efficacy endpoints from the Phase 3 DECIDE study comparing ZINBRYTA to AVONEX® (interferon beta-1a intramuscular (IM) injection) showed treatment with ZINBRYTA led to significant improvements across cognitive outcome measures. New 144-week data show mean improvements from baseline on the Symbol Digit Modalities Test (a measure of visual information processing speed and attention in patients) were +6.30 for ZINBRYTA-treated patients versus +3.09 for AVONEX-treated patients; p=0.0024.

Data from the SELECT and SELECTION Studies Provide Insight into Targeted and Reversible MOA of ZINBRYTA

A post-hoc analysis of results from SELECT and the extension study SELECTION evaluated the effects of ZINBRYTA on total and differential lymphocyte counts in patients who received ZINBRYTA continuously over two years, and in patients who were randomized to a 24-week washout period before completing treatment with ZINBRYTA in SELECTION.

"ZINBRYTA is an investigational therapy that is thought to work by regulating inflammation without broadly depleting the immune system – an important consideration for people living with the disease," said Ralph Kern, M.D., senior vice president, Worldwide Medical, Biogen. "ZINBRYTA has been shown to increase certain types of immunoregulatory cells and reduce cells that contribute to neurological injury caused by multiple sclerosis (MS)."

Results show the reversible effect of ZINBRYTA on immune cells and that it did not cause broad immune cell depletion:

- Decreases in total lymphocyte counts returned to baseline levels approximately eight 8 to 12 weeks upon treatment discontinuation
- Within six months of treatment discontinuation, all studied cell counts measured returned to baseline values in SELECT
- ZINBRYTA led to an increase in $CD56^{bright}$ natural killer (NK) cells, which help regulate the immune system:
    - At the end of the one-year SELECT study, mean $CD56^{bright}$ NK counts expanded by ~five-fold
- ZINBRYTA's targeted immunomodulatory MOA was further evidenced by the absence of broad depletion of total lymphocytes, CD4+ and CD8+ T-cells during treatment

Analysis Supports Safety Profile of ZINBRYTA

A post-hoc analysis of safety data from DECIDE demonstrated that 94 percent of cutaneous adverse events (AEs) associated with ZINBRYTA treatment in the study were mild or moderate in severity. Serious cutaneous AEs, which occurred in 2 percent of ZINBRYTA-treated patients, resolved following topical and/or systemic steroids, antihistamines, other therapies or treatment discontinuation. Biogen and AbbVie continue to examine cutaneous AEs more commonly associated with ZINBRYTA treatment.

A Complete List of ZINBRYTA AAN Data Presentations Includes:

- Improved Cognitive Outcomes in Relapsing-Remitting Multiple Sclerosis with Daclizumab HYP in the Phase 3 DECIDE Study – *Poster P3.090 – Monday, April 18, 8:30 a.m.-7 p.m. PT*
- Reversible Effects of Daclizumab HYP on Lymphocyte Counts in RRMS Patients: Data from the SELECT Trilogy Studies – *Poster P5.281 – Wednesday, April 20, 8:30 a.m.-7 p.m. PT*
- Experience with Serious Cutaneous Events in the DECIDE Study – *Poster P2.083 – Sunday, April 17, 8:30 a.m.-5:30 p.m. PT*
- Analysis of Relapse Events in the DECIDE Study Using a Novel Weighted Hurdle Model – *Poster P2.111 – Sunday, April 17, 8:30 a.m.-5:30 p.m. PT*
- Tentative and Confirmed Disability Progression in MS Clinical Trials – *Poster P2.115 – Sunday, April 17, 8:30 a.m.-5:30 p.m. PT*

- Effects of Daclizumab HYP on Accumulation of Disability Exclusive of Acute Relapse in Moderately/Severely Disabled Relapsing-Remitting Multiple Sclerosis Patients: Neurophysical Composite Outcome from the DECIDE Study – *Poster P3.085 – Monday, April 18, 8:30 a.m.-7 p.m. PT*

About the DECIDE Study
DECIDE was a two- to three-year, Phase 3, global, randomized, double-blind, multicenter study designed to determine if ZINBRYTA would provide superior outcomes for certain clinical endpoints compared to treatment with AVONEX (interferon beta-1a 30 mcg intramuscular (IM) injection). DECIDE was an active comparator study with two groups: 150 mg of subcutaneous (SC) ZINBRYTA every four weeks was compared to AVONEX 30 mcg IM once weekly.

In DECIDE, statistical significance was achieved on the primary endpoint of reduction in annualized relapse rate (ARR), as well as on the first secondary endpoint, the number of new or newly enlarging T2-hyperintense lesions. However, based on the primary prespecified analysis, statistical significance was not achieved on the secondary endpoint evaluating the proportion of patients with sustained disability progression as measured by the Expanded Disability Status Scale (EDSS) at 12 weeks. Additional secondary endpoints included the proportion of relapse-free patients and the proportion of patients who experienced a worsening physical impact score on the Multiple Sclerosis Impact Scale (MSIS-29).

The overall incidence of AEs was similar in the ZINBRYTA and AVONEX groups. In patients treated with ZINBRYTA compared to AVONEX, there was an increased incidence of serious infections (4 percent versus 2 percent), serious cutaneous reactions (2 percent versus <1 percent), and elevations of liver transaminases greater than five times the upper limit of normal (6 percent versus 3 percent).

About the SELECT Trilogy of Studies
The SELECT Trilogy (SELECT, SELECTION and SELECTED) of clinical studies was designed to evaluate the efficacy and safety of ZINBRYTA in patients with relapsing-remitting multiple sclerosis (RRMS). SELECT was a multicenter, randomized, double-blind, Phase 2 study that evaluated the efficacy and safety of ZINBRYTA 150 and 300 mg subcutaneous (SC) every four weeks for one year versus placebo. In SELECTION, a one-year double-blind extension of SELECT, placebo-treated patients were randomized to ZINBRYTA 150 or 300 mg SC, and ZINBRYTA-treated patients either continued their previous dosage of ZINBRYTA or underwent a 24-week washout period followed by re-initiation of ZINBRYTA at their previous dose. SELECTED is an ongoing, open-label, extension study of SELECTION that is being conducted to assess the long-term safety and efficacy of ZINBRYTA monotherapy (150 mg SC every four weeks).

About ZINBRYTA™ (daclizumab HYP)
ZINBRYTA (daclizumab HYP) is an investigational compound being developed for the treatment of relapsing forms of MS. ZINBRYTA is a new form of a humanized monoclonal antibody that selectively binds to the high-affinity interleukin-2 (IL-2) receptor subunit (CD25) that is expressed at high levels on T-cells that become activated in people with MS. ZINBRYTA modulates IL-2 signaling without causing general immune cell depletion.

ZINBRYTA is under regulatory review in the United States, the European Union, Switzerland, Canada and Australia. Biogen and AbbVie are jointly developing ZINBRYTA.

About Biogen
Through cutting-edge science and medicine, Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological, autoimmune and rare diseases. Founded in 1978, Biogen is one of the world's oldest independent biotechnology companies and patients worldwide benefit from its leading multiple sclerosis and innovative hemophilia therapies. For more information, please visit www.biogen.com. Follow us on Twitter.

Safe Harbor
This press release contains forward-looking statements, including statements about additional analyses of safety and efficacy data from clinical studies of ZINBRYTA, and potential impact of ZINBRYTA, if approved. These statements may be identified by words such as "believe," "expect," "may," "plan," "potential," "will" and similar expressions, and are based on Biogen's current beliefs and expectations. You should not place undue reliance on these statements. Drug development and commercialization involve a high degree of risk. Factors which could cause actual results to differ materially from Biogen's current expectations include the risk that unexpected concerns may arise from additional data or analysis, regulatory authorities may require additional data or information or further studies, or may fail to approve, or refuse to approve, or may delay approval of Biogen's drug candidates, including ZINBRYTA, or Biogen may encounter other unexpected hurdles. For more detailed information on the risks and uncertainties associated with Biogen's drug development and commercialization activities and risks relating to Biogen's collaborations with third parties, please review the Risk Factors section of Biogen's most recent annual or quarterly report filed with the Securities and Exchange Commission. Any forward-looking statements speak only as of the date of this press release and Biogen assumes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

About AbbVie
AbbVie is a global, research-based biopharmaceutical company formed in 2013 following separation from Abbott Laboratories. The company's mission is to use its expertise, dedicated people and unique approach to innovation to develop and market advanced therapies that address some of the world's most complex and serious diseases. Together with its wholly-owned subsidiary, Pharmacyclics, AbbVie employs more than 28,000 people worldwide and markets medicines in more than 170 countries. For further information on the company and its people, portfolio and commitments, please visit www.abbvie.com. Follow @abbvie on Twitter or view careers on our Facebook or LinkedIn page.

Forward-Looking Statements
Some statements in this news release may be forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995. The words "believe," "expect," "anticipate," "project" and similar expressions, among others, generally identify forward-looking statements. AbbVie cautions that these forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those indicated in the forward-looking statements. Such risks and uncertainties include, but are not limited to, challenges to intellectual property, competition from other products, difficulties inherent in the research and development process, adverse litigation or government action, and changes to laws and regulations applicable to our industry.

Additional information about the economic, competitive, governmental, technological and other factors that may affect AbbVie's operations is set forth in Item 1A, "Risk Factors," in AbbVie's 2014 Annual Report on Form 10-K, which has been filed with the Securities and Exchange Commission. AbbVie undertakes no obligation to release publicly any revisions to forward-looking statements as a result of subsequent events or developments, except as required by law.

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