Biogen and AbbVie's Once-Monthly ZINBRYTA™ (Daclizumab) Approved in European Union for Treatment of Multiple Sclerosis

July 5, 2016

- ZINBRYTA Significantly Reduced Multiple Measures of Disease Activity in Patients with Relapsing Forms of MS -

- Targeted Mechanism of Action of ZINBRYTA Did Not Cause Broad, Prolonged Depletion of Studied Immune Cell Types -

CAMBRIDGE, Mass. & NORTH CHICAGO, Ill.--(BUSINESS WIRE)--The European Commission (EC) has granted marketing authorization for ZINBRYTA™ (daclizumab) for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS)Biogen (NASDAQ: BIIB) and AbbVie (NYSE: ABBV) announced today. ZINBRYTA is a once-monthly, self-administered, subcutaneous injection.

"Clinical data showed ZINBRYTA significantly reduced relapses, 24-week confirmed disability progression and new brain lesions for up to three years compared to AVONEX® (interferon beta-1a) intramuscular injection, providing a valuable new option for people with RMS," said Professor Gavin Giovannoni, Chair of Neurology, Blizard Institute, Barts and The London School of Medicine and Dentistry. "ZINBRYTA has an immunomodulatory mechanism of action (MOA) that regulates inflammation without broadly depleting the immune system, and immune cell effects are reversible within six months. This offers an alternative approach to treating multiple sclerosis (MS) and is an important consideration when deciding how to sequence therapies throughout the course of a patient's disease."

The EC approval of ZINBRYTA is supported by results from two studies, including DECIDE, the largest and longest head-to-head Phase 3 study ever conducted in MS. The Phase 2b SELECT and Phase 3 DECIDE studies were global, randomized, double-blind, controlled studies that involved approximately 2,400 people living with RMS. Some patients in DECIDE were treated for up to three years.

In DECIDE and SELECT, ZINBRYTA significantly reduced patients' annualized relapse rate (ARR), the primary endpoint of the studies, by 45 percent compared to AVONEX up to 144 weeks and by 54 percent compared to placebo at 52 weeks (both $p<0.0001$), respectively. Analyses of these studies demonstrated the consistent effect of ZINBRYTA relative to placebo and AVONEX across various subgroups of patients defined by demographic and MS disease characteristics.

"With the approval of ZINBRYTA in the European Union, we are providing a much needed treatment option for people living with MS," said Michael Severino, M.D., executive vice president, research and development and chief scientific officer, AbbVie. "This is an important part of AbbVie's ongoing commitment to advancing neuroscience research specifically in the area of MS."

In addition to the statistically significant ARR, the Summary of Product Characteristics (SmPC) also includes the following ZINBRYTA clinical measures:

- Statistically significant effect on 24-week confirmed disability progression in ZINBRYTA-treated patients with a hazard ratio of 0.73 [95% Confidence Interval 0.55, 0.98].
- Statistically significant reduction in the number of new or newly enlarging T2 hyperintense lesions, the number of new T1 Gd-enhancing lesions and the mean number of new T1 hypointense lesions at 96 weeks.
- Reduced clinically meaningful worsening in the patient-reported physical impact of MS (≥7.5 point worsening from baseline to week 96 in the MSIS-29 physical score) compared to AVONEX.

"ZINBRYTA is an important new once-monthly option for people with RMS, including those whose disease activity has been insufficiently controlled by their prior therapy," said Alfred Sandrock, M.D., Ph.D., executive vice president and chief medical officer at Biogen. "MS manifests differently in each person, with varied symptoms and progressions; therefore, it is important that people living with the disease have treatment choices to address their diverse and evolving needs."

ZINBRYTA's MOA is thought to block the activation of autoreactive T-cells, a major contributor to inflammation in the nervous system of people with MS. ZINBRYTA leads to an increase in immunoregulatory $CD56^{bright}$ natural killer (NK) cells, which have been shown to selectively decrease activated T-cells that contribute to the nerve injury caused by MS. These immunomodulatory effects of ZINBRYTA are believed to reduce central nervous system pathology in MS and thereby reduce the occurrence of relapse and disability progression.

- During ZINBRYTA treatment, mean cell counts for the major immune subsets (T, B, and NK cells) remained within normal ranges; total lymphocyte, T and B cell counts decreased on average ≤10 percent from baseline during the first year of treatment.
- Total lymphocyte counts returned to baseline within approximately eight to 12 weeks after the last dose, and all other cell counts studied returned to baseline within approximately 20 to 24 weeks after the last dose.

Warnings and precautions include hepatic injury, skin reactions, depression, infections, gastro intestinal disorders, and lymphopenia. The most commonly reported adverse reactions leading to discontinuation in patients treated with ZINBRYTA were hepatic reactions, including elevations of serum transaminases (5%), and cutaneous reactions (4%). The most common adverse events that occurred in ZINBRYTA-treated patients were rash, increased alanine aminotransferase (a type of liver enzyme), depression, nasopharyngitis (inflammation of the nose and part of the throat), upper respiratory tract infection, influenza, oropharyngeal (part of the throat) pain and lymphadenopathy (enlargement of the lymph nodes).

About the DECIDE Study

DECIDE was a two- to three-year, Phase 3, global, randomized, double-blind, multicenter study in patients with relapsing forms of multiple sclerosis (RMS) 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 ZINBRYTA every four weeks (n=919) was compared to AVONEX IM once weekly (n=922).

About the SELECT Study

SELECT was a multicenter, randomized, double-blind, Phase 2b study that evaluated the efficacy and safety of ZINBRYTA 150 mg (n=208) and 300 mg (n=209) subcutaneous every four weeks for one year versus placebo (n=204) in patients with relapsing forms of multiple sclerosis (RMS).

About ZINBRYTA™ (daclizumab)

ZINBRYTA is being developed globally for relapsing forms of multiple sclerosis (RMS). The recommended dosage of ZINBRYTA is 150 mg, self-administered subcutaneously on a monthly basis. ZINBRYTA is also approved in the United States and is under regulatory review in Switzerland, Canada and Australia.

In clinical trials, ZINBRYTA demonstrated superior efficacy in relapse reduction and MRI, key measures of MS disease activity, compared to AVONEX® (interferon beta-1a) intramuscular injection and placebo. In the EU, an educational program to inform physicians and patients about the risk of severe hepatic injury and the procedures related to the appropriate management of this risk to minimize its occurrence and its severity.

ZINBRYTA is a humanized IgG1 monoclonal antibody that selectively binds to the high-affinity interleukin-2 (IL-2) receptor subunit (CD25). CD25 is expressed at high levels on T-cells that become activated in people with MS.

About Multiple Sclerosis

Multiple sclerosis (MS) is a chronic, often disabling disease that attacks the central nervous system, which is made up of the brain, spinal cord and optic nerves. Symptoms may be mild or severe, ranging from numbness in the limbs to paralysis or loss of vision. The progression, severity and specific symptoms of MS are unpredictable and vary from one person to another.[1] MS affects more than 2.3 million people worldwide.[1] Relapsing MS is the most common form of the disease, accounting for 85 percent of cases, and is characterized by clearly defined acute attacks with full recovery or with residual deficit upon recovery.[2]

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.

Biogen Safe Harbor

This press release includes forward-looking statements, including statements about the potential therapeutic effects and benefits of ZINBRYTA. These forward-looking statements may be accompanied by such words as "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "will," and other words and terms of similar meaning. You should not place undue reliance on these statements. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including uncertainty of success in commercialization of ZINBRYTA, which may be impacted by, among other things, slower than anticipated acceptance of ZINBRYTA by patients and the medical community, competition in the MS market, the effectiveness of sales and marketing efforts, problems with the manufacturing process for ZINBRYTA, the occurrence of adverse safety events, difficulties in obtaining or changes in the availability of reimbursement for ZINBRYTA and Biogen's other MS products, failure to obtain regulatory approvals in other 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 (SEC). 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.

AbbVie 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," of AbbVie's 2015 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.

[1] Multiple Sclerosis International Federation (MSIF). *What is MS?* Date accessed: June 27, 2016. http://www.msif.org/about-ms/what-is-ms/.

[2] MSIF. *Types of MS.* Date accessed: June 27, 2016. http://www.msif.org/about-ms/types-of-ms/.

Multimedia Files:

Download All Files
Preview image

Download:
Download Thumbnail (3.82 KB)
Download Preview (4.81 KB)
Download Small (16.94 KB)
Download Full Size (30.24 KB)
Download Square (4.9 KB)
Preview image

Download:
Download Thumbnail (3.14 KB)
Download Preview (6.96 KB)
Download Small (14.98 KB)
Download Square (7.93 KB)

Contact:

MEDIA CONTACT:
Biogen
Ligia Del Bianco, +1 781-464-3260
public.affairs@biogen.com
or
AbbVie
Jane Woo, +1 847-937-4754
jane.woo@abbvie.com
or
INVESTOR CONTACT:
Biogen
Mike Hencke, +1 781-464-2442
IR@biogen.com
or
AbbVie
Liz Shea, +1 847-935-2211
elizabeth.shea@abbvie.com