FDA Approves Biogen's TOFIDENCE™ (tocilizumab-bavi), a Biosimilar Referencing ACTEMRA®

September 29, 2023

- TOFIDENCE (BIIB800) becomes the first tocilizumab biosimilar to gain FDA approval in the United States
- FDA approval is based on a robust analytical, non-clinical and clinical data package comparing TOFIDENCE to the reference product ACTEMRA

CAMBRIDGE, Mass., Sept. 29, 2023 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) announced that the U.S. Food and Drug Administration (FDA) has approved TOFIDENCE (tocilizumab-bavi) intravenous formulation, a biosimilar monoclonal antibody referencing ACTEMRA. The TOFIDENCE intravenous formulation is approved for the treatment of moderately to severely active rheumatoid arthritis, polyarticular juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis.

TOFIDENCE is the first tocilizumab biosimilar approved in the United States. Biosimilars are biologic products that have been demonstrated to have equivalent efficacy and comparable safety as the approved reference product, with the advantage that they may offer cost savings and promote expanded and sustainable access to therapies. Spending on therapies for autoimmune diseases has consistently increased by 10%–25% each year over the past decade[1]. Since biosimilar entry in the US, medicines with biosimilar competition have experienced greater patient adoption equaling more than 150 million days of patient therapy[1].

"The approval of TOFIDENCE in the U.S. marks another positive step toward helping more people with chronic autoimmune conditions gain access to leading therapies," said Ian Henshaw, Global Head of Biosimilars at Biogen. "With the increasing numbers of approved biosimilars, we expect increased savings and sustainability for healthcare systems and an increase in physician choice and patient access to biologics."

Biogen and Bio-Thera entered into a commercialization and license agreement for TOFIDENCE (BAT1806/BIIB800) in April 2021. Developed by Bio-Thera, TOFIDENCE will be commercialized by Biogen in the United States. Under the agreement, Biogen has exclusive regulatory, manufacturing, and commercial rights to TOFIDENCE in all countries excluding China (including Hong Kong, Macau and Taiwan). Biogen is currently evaluating the potential launch timeline for TOFIDENCE in the U.S.

The FDA approval of TOFIDENCE was based on a comprehensive analytical, non-clinical and clinical data package submitted by Biogen to the FDA in Sept 2022. Extensive analytical characterization of the structural, physicochemical, and biological properties of TOFIDENCE was conducted and supports biosimilarity with the reference product. Additionally, a randomized double-blind, single-dose, three-arm, parallel phase I study compared the pharmacokinetics, safety and immunogenicity of TOFIDENCE with both the US and EU reference tocilizumab in healthy volunteers, while a randomized, double-blind, multi-dose, three-arm parallel phase III study compared TOFIDENCE with tocilizumab to establish equivalent efficacy and comparable pharmacokinetic, safety and immunogenicity profiles, in subjects with rheumatoid arthritis inadequately controlled by methotrexate. The totality of evidence demonstrated TOFIDENCE is a biosimilar of the reference biologic.

About TOFIDENCE (tocilizumab)
TOFIDENCE (tocilizumab), is a treatment developed as a biosimilar to the reference product ACTEMRA. TOFIDENCE is indicated for the treatment of moderately to severely active rheumatoid arthritis, polyarticular juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis.

Indications
Rheumatoid Arthritis (RA)
Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs).

Polyarticular Juvenile Idiopathic Arthritis (PJIA)
Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.

Systemic Juvenile Idiopathic Arthritis (SJIA)
Patients 2 years of age and older with active systemic juvenile idiopathic arthritis.

IMPORTANT SAFETY INFORMATION
The U.S. prescribing information for TOFIDENCE includes a boxed WARNING for RISK OF SERIOUS INFECTIONS: Patients treated with tocilizumab products including TOFIDENCE are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

If a serious infection develops, interrupt TOFIDENCE until the infection is controlled.

Reported infections include:

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before TOFIDENCE use and during therapy. Treatment for latent infection should be initiated prior to TOFIDENCE use.**
- **Invasive fungal infections, including candidiasis, aspergillosis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
- **Bacterial, viral and other infections due to opportunistic pathogens.**

The risks and benefits of treatment with TOFIDENCE should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with TOFIDENCE, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Contraindications
TOFIDENCE is contraindicated in patients with known hypersensitivity to tocilizumab products.

Warnings and Precautions
Serious Infections - do not administer TOFIDENCE during an active infection, including localized infections. If a serious infection develops, interrupt TOFIDENCE until the infection is controlled.

Gastrointestinal (GI) perforation - use with caution in patients who may be at increased risk.

Hepatotoxicity - Monitor patients for signs and symptoms of hepatic injury. Modify or discontinue TOFIDENCE if abnormal liver tests persist or worsen or if clinical signs and symptoms of liver disease develop.

Laboratory monitoring - recommended due to potential consequences of treatment-related changes in neutrophils, platelets, lipids, and liver function tests.

Hypersensitivity reactions, including anaphylaxis and death have occurred.

Live vaccines - Avoid use with TOFIDENCE.

Adverse Reactions
Most common adverse reactions (incidence of at least 5%): upper respiratory tract infections, nasopharyngitis, headache, hypertension, increased ALT.

For additional Important Safety Information on TOFIDENCE (tocilizumab-bavi), see full Prescribing Information.

About Biogen
Founded in 1978, Biogen is a leading global biotechnology company that has pioneered multiple breakthrough innovations including a broad portfolio of medicines to treat multiple sclerosis, the first approved treatment for spinal muscular atrophy, and two co-developed treatments to address a defining pathology of Alzheimer's disease. Biogen is advancing a pipeline of potential novel therapies across neurology, neuropsychiatry, specialized immunology and rare diseases and remains acutely focused on its purpose of serving humanity through science while advancing a healthier, more sustainable and equitable world.

We routinely post information that may be important to investors on our website at www.biogen.com. Follow us on social media - X, 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, relating to the potential benefits, safety and efficacy of TOFIDENCE; potential benefits of our collaboration with Bio-Thera; risks and uncertainties associated with drug development and commercialization; the potential of Biogen's commercial business and pipeline programs; Biogen's strategy and plans; and potential cost healthcare savings related to biosimilars. These forward-looking statements may be accompanied by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "potential," "possible," "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, risks that risks of unexpected costs or delays or other unexpected hurdles; uncertainty of success in the commercialization of TOFIDENCE, which may be impacted by, among other things, unexpected concerns that may arise from additional data or analysis, the occurrence of adverse safety events, failure to obtain regulatory approvals in certain jurisdictions, failure to protect and enforce data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; risks of legal actions, regulatory scrutiny or other challenges to biosimilars; the direct and indirect impacts of the ongoing COVID-19 pandemic on Biogen's business, results of operations and financial condition; the risks of doing business internationally, including currency exchange rate fluctuations; 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 Biogen's expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this news release. Biogen does not undertake any obligation to publicly update any forward-looking statements.

References:

1. Association for Accessible Medicines. The U.S. Generic & Biosimilars Medicines Savings Report, September 2022. https://accessiblemeds.org/sites/default/files/2022-09/AAM-2022-Generic-Biosimilar-Medicines-Savings-Report.pdf Accessed August 2023.

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