ENTYVIO® (VEDOLIZUMAB) SHOWS HIGHER RATES OF MUCOSAL HEALING VERSUS TNFα-ANTAGONIST THERAPY IN ULCERATIVE COLITIS AND CROHN'S DISEASE PATIENTS IN COMPARATIVE EFFECTIVENESS REAL-WORLD DATA ANALYSIS

OSAKA, Japan –New clinical study also provides data for Entyvio® in inducing complete mucosal healing and endoscopic remission, particularly in bio-naïve patients

Takeda Pharmaceutical Company Limited (TSE: 4502) ("Takeda") announced new real-world data evaluating the comparative effectiveness of Entyvio® (vedolizumab) and tumor necrosis factor-alpha (TNFα)-antagonist therapy in patients with moderately to severely active ulcerative colitis (UC) or Crohn's disease (CD). These data were presented as oral presentations at the 13th Congress of the European Crohn's and Colitis Organization (ECCO) from February 14 to 17, 2018 in Vienna, Austria. These analyses observed that patients with UC treated with Entyvio compared to TNFα-antagonist therapy had statistically significant higher 12-month cumulative rates of mucosal healing (50% vs 42%, hazard ratio [HR] 1.73, 95% confidence interval [CI] 1.10-2.73) and clinical remission (54% vs 37%; HR 1.54, 95% CI 1.08-2.18), and numerically higher steroid-free clinical remission rates (49% vs 38%; HR 1.43, 95% CI 0.79-2.60). In CD, results reported statistically significant higher 12-month cumulative rates of mucosal healing (50% vs 41%; HR 1.67, 95% CI 1.13-2.47), and numerically higher rates of clinical remission (38% vs 34%; HR 1.27, 95% CI 0.91-1.78) and steroid-free clinical remission (26% vs 18%; HR 1.75, 95% CI 0.90-3.43) compared to TNFα-antagonist therapy. These analyses were conducted by the VICTORY (Vedolizumab Health OuTComes in InflammatORY Bowel Diseases) Consortium.[1,2]

"These data from the VICTORY Consortium highlight the effectiveness of Entyvio in achieving mucosal healing and clinical remission in the real-world, and support the use of Entyvio as a first-line biologic therapy," said Professor William Sandborn, M.D., Chief, Division of Gastroenterology, University of California San Diego. "While additional research is needed to confirm these findings, these are important comparative effectiveness analyses of real-world data involving Entyvio and TNFα-antagonist therapy, which further aid our understanding of biologic therapy in clinical practice."

Of the 646 UC and 1,122 CD VICTORY Consortium patients, data from 334 UC (n=167 Entyvio patients; 49% male; median age 36 years) and 538 CD (n=269 Entyvio patients; 44% male; median age 35 years) were analyzed. Entyvio patients were matched (1:1)* to patients on anti-TNFα therapy using propensity scores to control for baseline differences between groups. Researchers used Cox proportional hazard models to compare cumulative rates of mucosal healing (absence of ulcers or erosions for CD; Mayo endoscopic sub-score of 0 or 1 for UC), clinical remission (complete resolution of symptoms based on Physician Global Assessment) and steroid-free clinical remission (on steroids at baseline, tapered off, no repeat steroid prescription for 4 weeks). Findings were reported after adjusting for concomitant steroid or immunomodulator use, disease location (CD study only; isolated small bowel, ileocolonic, isolated colonic), and number of prior TNFα-antagonists used.[1,2]

New clinical data also being presented at ECCO from the Phase 3b open-label prospective multicenter study (VERSIFY) evaluating the efficacy of Entyvio on complete mucosal healing (absence of ulcerations), endoscopic remission (Simple endoscopic score for CD [SES-CD] ≤4) and endoscopic response (50% decrease in SES-CD from baseline) provide insight into complete mucosal healing in CD. Results at week 26 found Entyvio induced complete mucosal healing (15%), endoscopic remission (12%) and endoscopic response (25%) in the overall population of CD patients, particularly in an anti-TNFα-naïve setting (complete mucosal healing 24%, endoscopic remission 20%, and endoscopic response 28%). The trial included 101 patients with moderately to severely active CD who had previously experienced treatment failure with corticosteroids, immunomodulators, and/or at least one TNFα-antagonist therapy. In this study, 46% of patients were categorized as having severe endoscopic activity at entry (SES-CD score of >15). Patients received Entyvio 300 mg intravenously at weeks 0, 2, 6, and then every 8 weeks for 26 weeks, followed by a 26-week extension period. Dose escalation was not permitted.[3]

"Endoscopic remission and mucosal healing are important targets in the management of Crohn's disease and ulcerative colitis, as they look beyond symptoms to show how disease activity could be impacting underlying bowel damage. The VERSIFY clinical study generated positive results in complete mucosal healing and endoscopic remission rates in Crohn's disease, particularly in anti-TNFα-naïve patients. Looking across the Entyvio data presented at ECCO, we're encouraged by the large compendium of data for Entyvio regarding endoscopic remission and mucosal healing in both clinical studies and the real-world setting," said Mona Khalid, Senior

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Director, Head of Evidence and Value Generation, Takeda Pharmaceuticals.

At this year's ECCO congress, Takeda sponsored 33 posters and presentations on Entyvio, including real-world analyses and clinical studies evaluating the impact of Entyvio on long-term remission, comparative efficacy/effectiveness, mucosal healing, resource utilization, and in special patient populations across CD and UC.

For a full list of poster titles and authors, visit: **ecco-ibd.eu/publications/congress-abstract-s/abstracts-2018.html**.

*Propensity score matching (1:1) accounting for baseline differences between groups including age, sex, prior UC/CD-related hospitalization within the previous year, disease history, disease extent, disease severity, steroid refractoriness or dependence and prior TNFα-antagonist failure.

About Entyvio® (vedolizumab)

Vedolizumab is a gut-selective immunosuppressive biologic.[4] It is a humanized monoclonal antibody that is designed to specifically antagonize the alpha4beta7 integrin, inhibiting the binding of alpha4beta7 integrin to intestinal mucosal addressin cell adhesion molecule 1 (MAdCAM-1) and fibronectin, but not vascular cell adhesion molecule 1 (VCAM-1).[5] MAdCAM-1 is preferentially expressed on blood vessels and lymph nodes of the gastrointestinal tract.[6] The alpha4beta7 integrin is expressed on a subset of circulating white blood cells.[5] These cells have been shown to play a role in mediating the inflammatory process in UC and CD.[5,7,8] By inhibiting alpha4beta7 integrin, vedolizumab may limit the ability of certain white blood cells to infiltrate gut tissues.[5]

About the VICTORY Consortium

The VICTORY (Vedolizumab Health OuTComes in InflammatORY Bowel Diseases) Consortium is a collaboration of 12 leading inflammatory bowel disease (IBD) centers from across the U.S. and represents the first large, well-characterized cohort of patients taking Entyvio in a real-world setting in the U.S. Patients included in the consortium were identified at each site through electronic medical record searches, review of clinical records, and/or queries of infusion center records. More than 1,700 UC and CD patients are now included in the consortium database, which was started when Entyvio was launched in the U.S. in 2014.

About Ulcerative Colitis and Crohn's Disease

Ulcerative colitis (UC) and Crohn's disease (CD) are two of the most common forms of inflammatory bowel disease (IBD).[9] Both UC and CD are chronic, relapsing, remitting, inflammatory conditions of the gastrointestinal (GI) tract that are often progressive in nature.[10,11] UC only involves the large intestine as opposed to CD which can affect any part of the GI tract from mouth to anus.[12,13] CD can also affect the entire thickness of the bowel wall, while UC only involves the innermost lining of the large intestine.[12] UC commonly presents with symptoms of abdominal discomfort, loose bowel movements, including blood or pus.[12,14] CD commonly presents with symptoms of abdominal pain, diarrhea, and weight loss.[10] The cause of UC or CD is not fully understood; however, recent research suggests hereditary, genetics, environmental factors, and/or an abnormal immune response to microbial antigens in genetically predisposed individuals can lead to UC or CD.[12,15,16]

Therapeutic Indications

Ulcerative colitis

Vedolizumab is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumor necrosis factor-alpha (TNFα) antagonist.

Crohn's disease

Vedolizumab is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumor necrosis factor-alpha (TNFα) antagonist.

Important Safety Information

Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Special warnings and special precautions for use

Vedolizumab should be administered by a healthcare professional equipped to manage hypersensitivity reactions, including anaphylaxis, if they occur. Appropriate monitoring and medical support measures should be available for immediate use when administering vedolizumab. Observe all patients during infusion and until the infusion is complete.

Infusion-related reactions

In clinical studies, infusion-related reactions (IRR) and hypersensitivity reactions have been reported, with the majority being mild to moderate

in severity. If a severe IRR, anaphylactic reaction, or other severe reaction occurs, administration of vedolizumab must be discontinued immediately and appropriate treatment initiated (e.g., epinephrine and antihistamines). If a mild to moderate IRR occurs, the infusion rate can be slowed or interrupted and appropriate treatment initiated (e.g., epinephrine and antihistamines). Once the mild or moderate IRR subsides, continue the infusion. Physicians should consider pre-treatment (e.g., with antihistamine, hydrocortisone and/or paracetamol) prior to the next infusion for patients with a history of mild to moderate IRR to vedolizumab, in order to minimize their risks.

Infections

Vedolizumab is a gut-selective integrin antagonist with no identified systemic immunosuppressive activity. Physicians should be aware of the potential increased risk of opportunistic infections or infections for which the gut is a defensive barrier. Vedolizumab treatment is not to be initiated in patients with active, severe infections such as tuberculosis, sepsis, cytomegalovirus, listeriosis, and opportunistic infections until the infections are controlled, and physicians should consider withholding treatment in patients who develop a severe infection while on chronic treatment with vedolizumab. Caution should be exercised when considering the use of vedolizumab in patients with a controlled chronic severe infection or a history of recurring severe infections. Patients should be monitored closely for infections before, during and after treatment. Before starting treatment with vedolizumab, screening for tuberculosis may be considered according to local practice. Some integrin antagonists and some systemic immunosuppressive agents have been associated with progressive multifocal leukoencephalopathy (PML), which is a rare and often fatal opportunistic infection caused by the John Cunningham (JC) virus. By binding to the α4β7 integrin expressed on gut-homing lymphocytes, vedolizumab exerts an immunosuppressive effect on the gut. Although no systemic immunosuppressive effect was noted in healthy subjects, the effects on systemic immune system function in patients with inflammatory bowel disease are not known. No cases of PML were reported in clinical studies of vedolizumab however, healthcare professionals should monitor patients on vedolizumab for any new onset or worsening of neurological signs and symptoms, and consider neurological referral if they occur. If PML is suspected, treatment with vedolizumab must be withheld; if confirmed, treatment must be permanently discontinued. Typical signs and symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body, clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. The progression of deficits usually leads to death or severe disability over weeks or months.

Malignancies

The risk of malignancy is increased in patients with ulcerative colitis and Crohn's disease. Immunomodulatory medicinal products may increase the risk of malignancy.

Prior and concurrent use of biological products

No vedolizumab clinical trial data are available for patients previously treated with natalizumab. Caution should be exercised when considering the use of vedolizumab in these patients. No clinical trial data for concomitant use of vedolizumab with biologic immunosuppressants are available. Therefore, the use of vedolizumab in such patients is not recommended.

Vaccinations

Prior to initiating treatment with vedolizumab all patients should be brought up to date with all recommended immunizations. Patients receiving vedolizumab may receive non-live vaccines (e.g., subunit or inactivated vaccines) and may receive live vaccines only if the benefits outweigh the risks.

Adverse reactions include: Nasopharyngitis, Headache, Arthralgia, Upper respiratory tract infection, Bronchitis, Influenza, Sinusitis, Cough, Oropharyngeal pain, Nausea, Rash, Pruritus, Back pain, Pain in extremities, Pyrexia, and Fatigue.

Please consult with your local regulatory agency for approved labeling in your country.

For U.S. audiences, please see the full Prescribing Information including Medication Guide for ENTYVIO.[17]

For EU audiences, please see the Summary of Product Characteristics (SmPC) for ENTYVIO.[4]

Takeda's Commitment to Gastroenterology

Gastrointestinal (GI) diseases can be complex, debilitating and life-changing. Recognizing this unmet need, Takeda and our collaboration partners have focused on improving the lives of patients through the delivery of innovative medicines and dedicated patient disease support programs for over 25 years. Takeda aspires to advance how patients manage their disease. Additionally, Takeda is leading in areas of gastroenterology associated with high unmet need, such as inflammatory bowel disease,

acid-related diseases and motility disorders. Our GI Research & Development team is also exploring solutions in celiac disease and liver diseases, as well as scientific advancements through microbiome therapies.

About Takeda Pharmaceutical Company Limited

Takeda Pharmaceutical Company Limited (TSE: 4502) is a global, research and development-driven pharmaceutical company committed to bringing better health and a brighter future to patients by translating science into life-changing medicines. Takeda focuses its R&D efforts on oncology, gastroenterology and neuroscience therapeutic areas plus vaccines. Takeda conducts R&D both internally and with partners to stay at the leading edge of innovation. Innovative products, especially in oncology and gastroenterology, as well as Takeda's presence in emerging markets, are currently fueling the growth of Takeda. Around 30,000 Takeda employees are committed to improving quality of life for patients, working with Takeda's partners in health care in more than 70 countries.

For more information, visit:
takeda.com/newsroom

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SOURCE: Takeda Pharmaceutical Company Limited

BASF LAUNCHES HEPAXA AS FIRST DEDICATED PRODUCT IN THE U.S. TO HELP PATIENTS MANAGE NON-ALCOHOLIC FATTY LIVER DISEASE

FLORHAM PARK, NJ and ANN ARBOR, MI – BASF Corporation is introducing HepaxaTM, a product that can help tens of millions of patients manage Non-Alcoholic Fatty Liver Disease (NAFLD), one of the most common forms of chronic liver disease. Providing highly concentrated and pure eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), Hepaxa is the first product in the U.S. specifically designed to address a buildup of fat in the liver, known as steatosis, in NAFLD patients. Hepaxa will be distributed nationally through DIEM Labs, LLC.

Studies have shown that NAFLD patients are deficient in EPA and DHA. Hepaxa increases the levels of these important fatty acids in the blood, which improves the liver's ability to process excessive fat stored there while inhibiting the conversion of dietary carbohydrates into fat.

A 2017 BASF study has shown that Hepaxa is effective and safe in the dietary management of NAFLD patients. BASF plans to publish the clinical results of this product-specific human intervention trial in the second half of 2018.

Hepaxa is manufactured using a patented purification technology removing persistent organic pollutants and other unwanted lipids such as cholesterol, which are naturally found in all fish oil-based products. Research has shown that one specific pollutant, PCB 153, is particularly harmful to NAFLD patients. The liver function of NAFLD patients is compromised and it is important to avoid additional exposure to unwanted components of traditional fish oil.

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"BASF's launch of Hepaxa is the result of our research and development efforts targeting liver health, where we are capitalizing on our unique scientific competencies," says Christoph Garbotz, Head of Commercial Management Advanced Health Solutions, BASF. "With NAFLD rapidly becoming a major public health concern worldwide, we are proud to now offer this first-to-market, dedicated solution for NAFLD patients in the U.S."

"Hepaxa is uniquely positioned to support the dietary management of steatosis in NAFLD patients," says Tim Prince, Director of Sales at DIEM Labs. "Healthcare providers are continuously looking for an adjunctive treatment to exercise and weight loss therapy to recommend to their patients. Hepaxa can now be used to begin turning around NAFLD in as little as six months."

Hepaxa is available as a medical food product in the U.S. to NAFLD patients 10 years and older for use under physician supervision. Physicians and healthcare professionals may request clinical support literature and product samples, and patients can gather information to share with their physicians, at: **Hepaxa-USA.com**.

About BASF

BASF Corporation, headquartered in Florham Park, New Jersey, is the North American affiliate of BASF SE, Ludwigshafen, Germany. BASF has nearly 17,500 employees in North America, and had sales of $16.2 billion in 2016. For more information about BASF's North American operations, visit www.basf.com.

At BASF, we create chemistry for a sustainable future. We combine economic success with environmental protection and social responsibility. The approximately 114,000 employees in the BASF Group work on contributing to the success of our customers in nearly all sectors and almost every country in the world. Our portfolio is organized into five segments: Chemicals, Performance Products, Functional Materials & Solutions, Agricultural Solutions and Oil & Gas. BASF generated sales of about €58 billion in 2016. BASF shares are traded on the stock exchanges in Frankfurt (BAS), London (BFA) and Zurich (BAS).

For further information, visit:
basf.com

About DIEM Labs

Diem Labs is a specialized medical food company committed to providing clinicians and consumers with clinically validated solutions for underserved and emerging health conditions. Formed by an international partnership of scientists, producers, and veterans of the US healthcare industry, Diem Labs is driven to supply safe and effective nutritional products that are supported by rigorous scientific evidence and meet the highest quality standards. Diem Labs' directors bring over 60 years of combined experience serving practitioners and patients through physician-direct and consumer-direct channels. Through strategic partnerships and proprietary development expertise, Diem Labs is dedicated to providing healthcare practitioners, patients and consumers with exclusive, effective solutions that address common challenges not met by products currently available in the healthcare marketplace.

Find more information at:
DiemLabsLLC.com

CRH MEDICAL CONFIRMS THAT ANCILLARY OPPORTUNITIES ARE IMPERATIVE TO WITHSTANDING GI REIMBURSEMENT PRESSURES

Join CRH Medical Corporation to learn more about the ancillary opportunities available to gastroenterologists at Digestive Disease Week on Monday, June 4th at 1:15 pm in the DDW Product Theater. Speakers Jay Kreger, President of CRH Anesthesia, and Dr. Mitchel Guttenplan, Medical Director for CRH Medical Corporation, discuss. Lunch will be provided.

CRH Medical offers both anesthesia partnerships and hemorrhoidal banding, offsetting reimbursement cuts in core GI businesses. Despite CMS cuts, CRH Anesthesia still provides supplemental income to GI practices while raising patient satisfaction. The CRH O'Regan System® provides safe and effective non-surgical treatment of hemorrhoids with favorable margins, performed by gastroenterologists and advanced practitioners alike.

For further information, visit:
crhmedicalproducts.com