CRH MEDICAL CORPORATION

Withstanding GI Reimbursement Pressures

Join CRH Medical Corporation to learn more about the ancillary opportunities available to gastroenterologists at the **ACG Annual Meeting 2018 on Monday, October 8 at 12:45 pm** in the ACG Product Theater. Speakers Jay Kreger, President of CRH Anesthesia, and Dr. Mitchel Guttenplan, Medical Director for CRH Medical Corporation, discuss. Lunch will be provided and your attendance enters you in a draw to win an iPad Pro.

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.

NEW PHASE 3 DATA SHOW INVESTIGATIONAL SUBCUTANEOUS FORMULATION OF VEDOLIZUMAB MEETS PRIMARY ENDPOINT IN ACHIEVING CLINICAL REMISSION AT WEEK 52 IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

Data to be discussed with global health authorities, including the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA)

Osaka, Japan– Takeda Pharmaceutical Company Limited [TSE:4502] ("Takeda") announced top-line results from the VISIBLE 1 clinical trial evaluating the efficacy and safety of an investigational subcutaneous (SC) formulation of vedolizumab for maintenance therapy in adult patients with moderately to severely active ulcerative colitis (UC) who achieved clinical response at week 6 following two doses of open-label vedolizumab intravenous (IV) induction therapy. In the primary endpoint of the trial, a statistically significant proportion of patients receiving vedolizumab SC beginning at week 6 and every two weeks following achieved clinical remission at week 52 compared to placebo. The safety data were consistent with the known safety profile of vedolizumab, and no new safety signals were identified. Further data from the trial will be presented at a future scientific congress.

"Meeting the primary endpoint of the VISIBLE 1 trial marks an exciting milestone in our approach to developing new ways to meet the needs of the ulcerative colitis patient community," said Asit Parikh, MD PhD, Head of Takeda's Gastroenterology Therapeutic Area Unit. "These results are encouraging and build on vedolizumab's robust clinical profile with more than 200,000 patient years of exposure. We plan to discuss these data with health authorities with the aim of bringing this innovative treatment option to patients."

VISIBLE 1 is a pivotal phase 3, randomized, double-dummy, double-blind, placebo-controlled study, with a vedolizumab IV reference arm, to evaluate the safety and efficacy of an investigational SC formulation of vedolizumab as maintenance therapy in adult patients with moderately to severely active UC who have achieved clinical response at week 6 following two doses of open-label vedolizumab IV therapy at weeks 0 and 2. The study enrolled 384 patients, all of whom had inadequate response with, loss of response to, or intolerance to corticosteroids, immunomodulators, or tumor necrosis factor-alpha (TNFα)-antagonist therapy prior to being enrolled. Patients who achieved clinical response at week 6 were randomized into one of three treatment groups, vedolizumab SC 108 mg and placebo IV, vedolizumab IV 300 mg and placebo SC, or placebo SC and placebo IV. Subcutaneous doses were administered every two weeks and intravenous doses were administered every eight weeks.

Additional endpoints assessed in VISIBLE 1 include the proportion of subjects achieving mucosal healing at week 52, durable clinical response, durable clinical remission and corticosteroid-free clinical remission at week 52.

About the VISIBLE clinical trial program

The VISIBLE clinical trial program aims to assess the efficacy and safety of an investigational subcutaneous (SC) formulation of vedolizumab as maintenance therapy in adult patients with moderately to severely active ulcerative colitis (UC) and Crohn's disease (CD). VISIBLE consists of three phase 3 studies involving over 1,000 patients which includes two randomized, double-blind, placebo-controlled studies examining the percentage of participants achieving clinical remission at week 52 in UC and CD respectively, and an open-label extension study to determine the long-term safety and efficacy of vedolizumab SC consisting of patients who have completed one of the randomized clinical trials.

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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). Both UC and CD are chronic, relapsing, remitting, inflammatory conditions of the gastrointestinal (GI) tract that are often progressive in nature. UC only involves the large intestine as opposed to CD which can affect any part of the GI tract from mouth to anus. CD can also affect the entire thickness of the bowel wall, while UC only involves the innermost lining of the large intestine. UC commonly presents with symptoms of abdominal discomfort, loose bowel movements, including blood or pus. CD commonly presents with symptoms of abdominal pain, diarrhea, and weight loss. 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.

About Entyvio® (vedolizumab)

Vedolizumab is a gut-selective biologic and is approved as an intravenous (IV) formulation. It is a humanized monoclonal antibody designed to specifically antagonize the alpha4beta7 integrin, inhibiting the binding of alpha4beta7 integrin to intestinal mucosal addressin cell adhesion molecule 1 (MAdCAM-1), but not vascular cell adhesion molecule 1 (VCAM-1). MAdCAM-1 is preferentially expressed on blood vessels and lymph nodes of the gastrointestinal tract. The alpha4beta7 integrin is expressed on a subset of circulating white blood cells. These cells have been shown to play a role in mediating the inflammatory process in ulcerative colitis (UC) and Crohn's disease (CD). By inhibiting alpha4beta7 integrin, vedolizumab may limit the ability of certain white blood cells to infiltrate gut tissues. Vedolizumab IV is approved for the treatment of adult patients with moderately to severely active UC and CD, 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. Vedolizumab IV has been granted marketing authorization in over 60 countries, including the United States and European Union, with over 200,000 patient years of exposure to date.

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.

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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®:

general.takedapharm.com/ENTYVIOPI
general.takedapharm.com/ENTYVIOMG

For EU audiences, please see the Summary of Product Characteristics (SmPC) for ENTYVIO®:

ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002782/WC500168528.pdf

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

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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

COMPULINK LAUNCHES ADVANTAGE SMART PRACTICE™ SUITE OF ARTIFICIAL INTELLIGENCE SOLUTIONS

Newbury Park, CA—Compulink Healthcare Solutions, a nationally recognized leader of specialty-specific EHR and Practice Management solutions announced the rollout of new artificial intelligence (AI)-enabled features in a release its calling Advantage SMART Practice.

Advantage uses AI technology and real-time data from the clinic to completely automate tasks such as billing, along with eliminating steps to improve patient flow.

AI-driven enhancements include:

- Advantage SMART Workflow™: Advantage knows which patients are being seen based on their room assignment and automatically displays their record when needed. The system also lets providers and staff know who is waiting, where they need to go next, and keeps them constantly informed for maximum efficiency.
- SMART Automated Billing, Eligibility & ERA Posting: Using the Advantage PracticeWatch™ task automation engine, staff can schedule eligibility, claims submission, and remittance posting to run unattended. Advantage also automatically populates a claim edit worklist to quickly identify and correct issues.
- Advantage SMART Patient Engagement™: Advantage automatically communicates personalized content directly to the patient's mobile device. This includes information about products and services specific to each individual patient as they arrive at the office and move through the normal patient workflow.

"We expect this release to take our client's efficiency across their entire clinic to a whole new level," said Link Wilson, CEO and founder of Compulink. "Our SMART billing features will reduce the amount of time required to generate and work claims by about 90%. With our SMART workflow engine, we're looking for patient throughput to increase by as much as 15% or more. And with our mobile patient engagement, the ability to engage patients in their own care while growing your patient base is really limitless."

The company's 2015 ONC Certified system is used by more than 20,000 providers in over 4,700 locations. Built on a single database, the Advantage all-in-one solution includes specialty-specific EHR for 19 specialties, along with practice management, Optical POS (for eyecare), inventory management, data analytics, patient engagement, and telehealth services. The company also offers solutions for ambulatory surgical centers (ASC) and provides an expert revenue cycle management service for its clients.

For more information and a product demonstration please contact Compulink at 800-456-4522 or visit:
compulinkadvantage.com