UCB News

For media

UCB announces U.S. FDA approval of RYSTIGGO® (rozanolixizumab-noli) for the treatment of adults with generalized myasthenia gravis

- FDA approval of RYSTIGGO® (rozanolixizumab-noli) has been granted under the Priority Review designation for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive[1]
- U.S. FDA approval is based on the pivotal Phase 3 MycarinG study in gMG[2], a large phase 3 study which demonstrated treatment with rozanolixizumab-noli resulted in statistically significant improvements in gMG-specific outcomes, including everyday activities such as breathing, talking, swallowing, and being able to rise from a chair[3]
- Additional treatment option provides opportunity for U.S. clinicians to tailor therapeutic approach based on individual patient needs

Brussels (Belgium) June 27 2023, 07:00: (CET) Regulated Information – Inside Information – UCB (Euronext Brussels: UCB), a global biopharmaceutical company, today announced RYSTIGGO® (rozanolixizumab-noli)* has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.[1]

Rozanolixizumab-noli injection for subcutaneous infusion is a humanized IgG4 monoclonal antibody that binds to the neonatal Fc receptor (FcRN), resulting in the reduction of circulating IgG.[1,4] It is the only FDA-approved treatment in adults for both anti-AChR and anti-MuSK antibody-positive gMG, the two most common subtypes of gMG.

"gMG can cause unpredictable fluctuations in severity and frequency of symptoms, which are often debilitating and can substantially impact the lives of patients. People living with gMG often face treatment options that are broad-acting, and that have traditionally only offered symptomatic relief" , explained Professor Vera Bril, Professor of Medicine (Neurology), University of Toronto, Director of the Neuromuscular Section, Division of Neurology, University of Toronto and University Health Network, Toronto, and lead investigator of the MycarinG study. "*There is a significant need for new, innovative treatment options to reduce the day-to-day burden of gMG. Rozanolixizumab-noli is a new treatment option, targeting one of the mechanisms of disease to provide symptom improvement in patient-and physician reported outcomes at day 43."*

gMG is a rare, chronic, heterogeneous (phenotypic and pathogenic), unpredictable autoimmune disease characterized by dysfunction and damage at the neuromuscular junction (NMJ).[5,6,7] Several factors are understood to be drivers of gMG disease pathology, including complement-cascade, immune cells and pathogenic IgG autoantibodies. Pathogenic IgG autoantibodies can impair synaptic transmission at the NMJ by targeting specific proteins on the post-synaptic membrane[6,7] This disrupts the ability of the nerves to stimulate the muscle and results in a weaker contraction.[7] gMG has a global prevalence of 100–350 cases per every 1 million people.[7,8]

"No two people living with gMG experience the disease in the same way, so we can't take a 'one size fits all' approach to disease management," said Iris Loew-Friedrich, Executive Vice-President and Chief Medical Officer at UCB. *"Disease management should be based on the clinical needs and preferences of the individual patient, and the aim of treatment is to help restore that patient's ability to carry out activities of daily living. The approval of rozanolixizumab-noli means doctors have an additional approved treatment option for their gMG patients who have not yet found a treatment that meets their needs."*

The FDA approval[1] is supported by safety and efficacy data from the pivotal Phase 3 MycarinG study (NCT03971422), published in *The Lancet Neurology* in May 2023[2]. The primary efficacy endpoint was the comparison of the change from baseline between treatment groups in the MG-ADL total score at day 43. MG-ADL is a measurement tool which assesses the impact of gMG on daily functions of 8 signs or symptoms that are typically affected in gMG. These include activities such as breathing, talking, swallowing, and being able to rise from a chair[3]. Each item is assessed on a 4-point scale where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment. A statistically significant difference favoring rozanolixizumab-noli was observed in the MG-ADL total score change from baseline [-3.4 points in rozanolixizumab-noli-treated group at either dose vs -0.8 points in the placebo-treated group ($p<0.001$)].

The secondary endpoint was the change between treatment groups from baseline to day 43 in the QMG. The QMG is a 13-item categorical grading system that assesses muscle weakness. Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment. A statistically significant difference favoring rozanolixizumab-noli was observed in the QMG total score change from baseline [-5.4 points and -6.7 points in rozanolixizumab-noli-treated group at ≈7mg/kg and ≈10 mg/kg dose level, respectively, vs -1.9 points in the placebo-treated group ($p<0.001$)].

The most common adverse reactions (reported in at least 10% of patients treated with in rozanolixizumab-noli) were headache, infections, diarrhea, pyrexia, hypersensitivity reactions, and nausea.[1]

"*We want to thank UCB for their continued commitment to the MG community to bring a new FDA-approved treatment option for generalized myasthenia gravis to patients and their treating physicians,"* said Samantha Masterson, President and Chief Executive Officer of the Myasthenia Gravis Foundation of America (MGFA). *"People living with generalized myasthenia gravis continue to experience significant unmet medical needs, this means expanding the number of FDA-approved treatment options is particularly important to treat this chronic, autoimmune, neuromuscular disease."*

Rozanolixizumab-noli will be commercially available in the U.S. during the 3rd quarter of 2023.

"Building on our decades of experience in neurology and immunology, we are proud to support the MG community with solutions to help improve patient lives, including a new FDA-approved treatment, education and support", continued Iris Loew-Friedrich. *The approval following priority review of rozanolixizumab-noli is a testament to this medicine's potential as a generally well-tolerated treatment option that is targeted to the individual needs of patients. We are so grateful to the patients, care partners, and investigators who participated in the MycarinG study, and to our employees and collaborators, whose dedication and commitment to the MG community made this important milestone possible."*

The FDA reviewed rozanolixizumab-noli under Priority Review. Rozanolixizumab is also currently under review by the European Medicines Agency (EMA) and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) for the treatment of adults with gMG. In 2019, the U.S. FDA granted orphan drug designation to rozanolixizumab-noli for the treatment of generalized myasthenia gravis.[9] Orphan designation was granted by the European Commission in April 2020 to rozanolixizumab for the treatment of generalized myasthenia gravis.[10] The PMDA granted similar orphan status to rozanolixizumab in Japan in November.[11] Responses from regulatory agencies to these submissions are expected by H1 2024.

About Generalized Myasthenia Gravis (gMG)

gMG is a rare disease with a global prevalence of 100–350 cases per every 1 million people.[7] People living with gMG can experience a variety of symptoms, including severe muscular weakness that can result in life-threatening weakness of the muscles of respiration, double vision, drooping eyelids, and difficulty swallowing, chewing and talking.[12,13]

In gMG, pathogenic autoantibodies can impair synaptic transmission at the neuromuscular junction (NMJ) by targeting specific proteins on the post-synaptic membrane.[4,5] This disrupts the ability of the nerves to stimulate the muscle and results in a weaker contraction. gMG can occur in any race, gender or age.[14]

About the MycarinG study[2]

The MycarinG study (NCT03971422) is a multi-center, Phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of rozanolixizumab in adult patients with gMG, with an open-label extension.

The primary endpoint for the MycarinG study is change in the Myasthenia Gravis-Activities of Daily Living Profile (MG-ADL) score, an eight-item patient-reported scale developed to assess MG symptoms and their effects on daily activities. Additional endpoints include response rates, changes in the Myasthenia Gravis composite (MGC) score, the Quantitative MG (QMG) score, patient-reported outcomes at day 43 and adverse events (AEs). The majority of patients taking part in the MycarinG study opted to enroll in any future extensions to this clinical trial. As a result, UCB is exploring the potential for further extension studies into this treatment.

For more information about the trial, visit https://clinicaltrials.gov/ct2/show/NCT03971422.

About rozanolixizumab

Rozanolixizumab is a subcutaneous administered, humanized monoclonal antibody that specifically binds, with high affinity, to human neonatal Fc receptor (FcRn). It has been designed to block the interaction of FcRn and Immunoglobulin G (IgG), accelerating the catabolism of antibodies and reducing the concentration of pathogenic IgG autoantibodies.[4]

Outside of the U.S. rozanolixizumab is not approved for use in any indication by any other regulatory authority worldwide.

*In the U.S., the International Nonproprietary Name (INN) for rozanolixizumab is 'rozanolixizumab-noli' following the FDA's 'Non-proprietary Naming of Biological Products Guidance'. This guidance advises that the nonproprietary name designated for originator biological products should be a proper name that is a

combination of the core name and a distinguishing suffix that is devoid of meaning and composed of four lowercase letters.

Important Safety Information for RYSTIGGO®

WARNINGS AND PRECAUTIONS

Infections: RYSTIGGO may increase the risk of infection. Delay RYSTIGGO administration in patients with an active infection until the infection is resolved. During treatment with RYSTIGGO, monitor for clinical signs and symptoms of infection. If serious infection occurs, administer appropriate treatment and consider withholding RYSTIGGO until the infection has resolved.

Immunization

Immunization with vaccines during RYSTIGGO treatment has not been studied. The safety of immunization with live or live-attenuated vaccines and the response to immunization with any vaccine are unknown. Because RYSTIGGO causes a reduction in IgG levels, vaccination with live-attenuated or live vaccines is not recommended during treatment with RYSTIGGO. Evaluate the need to administer age-appropriate vaccines according to immunization guidelines before initiation of a new treatment cycle with RYSTIGGO.

Aseptic Meningitis: Serious adverse reactions of aseptic meningitis (also called drug-induced aseptic meningitis) have been reported in patients treated with RYSTIGGO. If symptoms consistent with aseptic meningitis develop, diagnostic workup and treatment should be initiated according to the standard of care.

Hypersensitivity Reactions: Hypersensitivity reactions, including angioedema and rash, were observed in patients treated with RYSTIGGO. Management of hypersensitivity reactions depends on the type and severity of the reaction. Monitor patients during treatment with RYSTIGGO and for 15 minutes after for clinical signs and symptoms of hypersensitivity reactions. If a reaction occurs, institute appropriate measures if needed.

ADVERSE REACTIONS

In a placebo-controlled study, the most common adverse reactions (reported in at least 10% of RYSTIGGO-treated patients) were headache, infections, diarrhea, pyrexia, hypersensitivity reactions, and nausea. Serious infections were reported in 4% of patients treated with RYSTIGGO. Three fatal cases of pneumonia were identified, caused by COVID-19 infection in two patients and an unknown pathogen in one patient. Six cases of infections led to discontinuation of RYSTIGGO.

Full Prescribing Information will be available at https://www.ucb-usa.com/RYSTIGGO-prescribing-information.pdf

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About UCB

UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With approximately 8,600 people in approximately 40 countries, the company generated revenue of €5.5 billion in 2022. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news.

Forward looking statements

This press release may contain forward-looking statements including, without limitation, statements containing the words "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "continue" and similar expressions. These forward-looking statements are based on current plans, estimates and beliefs of management. All statements, other than statements of historical facts, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, arbitration, political, regulatory or clinical results or practices and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to known and unknown risks, uncertainties and assumptions which might cause the actual results, financial condition, performance or achievements of UCB, or industry results, to differ materially from those that may be expressed or implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: the global spread and impact of COVID-19, changes in general economic, business and competitive conditions, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms or within expected timing, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, product liability claims, challenges to patent protection for products or product candidates, competition from other products including biosimilars, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws, and hiring and retention of its employees. There is no guarantee that new product candidates will be discovered or identified in the pipeline, will progress to product approval or that new indications for existing products will be developed and approved. Movement from concept to commercial product is uncertain; preclinical results do not guarantee safety and efficacy of product candidates in humans. So far, the complexity of the human body cannot be reproduced in computer models, cell culture systems or animal models. The length of the timing to complete clinical trials and to get regulatory approval for product

marketing has varied in the past and UCB expects similar unpredictability going forward. Products or potential products, which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences disputes between the partners or may prove to be not as safe, effective or commercially successful as UCB may have believed at the start of such partnership. UCB's efforts to acquire other products or companies and to integrate the operations of such acquired companies may not be as successful as UCB may have believed at the moment of acquisition. Also, UCB or others could discover safety, side effects or manufacturing problems with its products and/or devices after they are marketed. The discovery of significant problems with a product similar to one of UCB's products that implicate an entire class of products may have a material adverse effect on sales of the entire class of affected products. Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment, including pricing pressure, political and public scrutiny, customer and prescriber patterns or practices, and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement activities and outcomes. Finally, a breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of UCB's data and systems.
Given these uncertainties, you should not place undue reliance on any of such forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labelling in any market, or at any particular time, nor can there be any guarantee that such products will be or will continue to be commercially successful in the future.

UCB is providing this information, including forward-looking statements, only as of the date of this press release and it does not reflect any potential impact from the evolving COVID-19 pandemic, unless indicated otherwise. UCB is following the worldwide developments diligently to assess the financial significance of this pandemic to UCB. UCB expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report or reflect any change in its forward-looking statements with regard thereto or any change in events, conditions or circumstances on which any such statement is based, unless such statement is required pursuant to applicable laws and regulations.

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